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Requester's Full Name: Springfield (STIC) Examiner #: 71976 Date: 7/15/02  
 Art Unit: 1645 Phone Number 305 3394 Serial Number: 91955739  
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\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Urease-based Vaccine + Treatment for Helicobacter Infection  
 Inventors (please provide full names): Pierre Michetti, Irene Cortesio-Thoulaz, Andre Blum, Catherine Davin, Rainer Haas, Jean-Pierre  
 Earliest Priority Filing Date: 2/23/94 / Kraehenbuhl, Emilia Saraga

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Method to treat gastroduodenal disease, administer  
Helicobacter urease peptides.  
urease B peptide.

Search diseases include: gastritis, peptic ulcer disease,  
 chronic dyspepsia, severe erosive gastroduodenitis,  
 refractory non-ulcer dyspepsia, intestinal metaplasia,  
 low grade MALT lymphoma, Helicobacter infection,  
Helicobacter pylori infection, H. felis disease  
urease, urease B, Helicobacter urease  
H. pylori urease

Search author/inventor names

THANKS  
 Springfield

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## Type of Search

## Vendors and cost where applicable

Searcher: <u>M. Smith</u>	NA Sequence (#) _____	STN _____
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: <u>07/16/02</u>	Bibliographic <u>X</u>	Dr. Link _____
Date Completed: <u>07/23/02</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: <u>65</u>	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: <u>70</u>	Other _____	Other (specify) _____

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L2 540 SEA FILE=HCAPLUS ((BLUM A?) OR (BLUM,A?) OR (BLUM, A?))/AU,IN  
L3 6 SEA FILE=HCAPLUS ((DAVIN C?) OR (DAVIN,C?) OR (DAVIN, C?))/AU,IN  
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L5 169 SEA FILE=HCAPLUS ("KRAEHENBUHL J P"/AU OR "KRAEHENBUHL JEAN P"/AU OR "KRAEHENBUHL JEAN PIERRE"/AU OR "KRAEHENBUHL JEAN PIERRE"/IN)  
L6 18 SEA FILE=HCAPLUS ("SARAGA E"/AU OR "SARAGA EMILIA"/AU OR "SARAGA EMILIA"/IN OR "SARAGA EMILIA P"/AU)  
L7 31 SEA FILE=HCAPLUS "CORTHESEY IRENE"/AU OR ("CORTHESEY THEULAZ I"/AU OR "CORTHESEY THEULAZ I E"/AU OR "CORTHESEY THEULAZ IRENE"/AU OR "CORTHESEY THEULAZ IRENE"/IN OR "CORTHESEY THEULAZ IRENE E"/AU)  
L8 1381 SEA FILE=HCAPLUS L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7  
L9 119 SEA FILE=HCAPLUS L8 AND (GASTR? OR ULCER?)  
L10 36 SEA FILE=HCAPLUS L9 AND HELICOBACT?

=> d ibib abs hitrn l10 1-36

L10 ANSWER 1 OF 36 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:489737 HCAPLUS  
TITLE: Essential role of ferritin Pfr in **Helicobacter**

pylori iron metabolism and **gastric** colonization

AUTHOR(S): Waidner, Barbara; Greiner, Stefan; Odenbreit, Stefan; Kavermann, Holger; Velayudhan, Jyoti; Stahler, Frank; Guhl, Johannes; Bisse, Emmanuel; Van Vliet, Arnoud H. M.; Andrews, Simon C.; Kusters, Johannes G.; Kelly, David J.; **Haas, Rainer**; Kist, Manfred; Bereswill, Stefan

CORPORATE SOURCE: Institute of Medical Microbiology and Hygiene, Department of Medical Microbiology and Hygiene, University Hospital of Freiburg, Freiburg, D-79104, Germany

SOURCE: Infection and Immunity (2002), 70(7), 3923-3929  
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The reactivity of the essential element iron necessitates a concerted expression of ferritins, which mediate iron storage in a nonreactive state. Here we have further established the role of the **Helicobacter pylori** ferritin Pfr in iron metab. and **gastric** colonization. Iron stored in Pfr enabled H. pylori to multiply under severe iron starvation and protected the bacteria from acid-amplified iron toxicity, as inactivation of the pfr gene restricted growth of H. pylori under these conditions. The lowered total iron content in the pfr mutant, which is probably caused by decreased iron uptake rates, was also reflected by an increased resistance to superoxide stress. Iron induction of Pfr synthesis was clearly diminished in an H. pylori feoB mutant, which lacked high-affinity ferrous iron transport, confirming that Pfr expression is mediated by changes in the cytoplasmic iron pool and not by extracellular iron. This is well in agreement with the recent discovery that iron induces Pfr synthesis by abolishing Fur-mediated repression of pfr transcription, which was further confirmed here by the observation that iron inhibited the in vitro binding of recombinant H. pylori Fur to the pfr promoter region. The functions of H. pylori Pfr in iron metab. are essential for survival in the **gastric** mucosa, as the pfr mutant was unable to colonize in a Mongolian gerbil-based animal model. In summary, the pfr phenotypes obsd. give new insights into prokaryotic ferritin functions and indicate that iron storage and homeostasis are of extraordinary importance for H. pylori to survive in its hostile natural environment.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:225421 HCAPLUS

DOCUMENT NUMBER: 136:351799

TITLE: Activation of **Helicobacter pylori** CagA by tyrosine phosphorylation is essential for dephosphorylation of host cell proteins in **gastric** epithelial cells

AUTHOR(S): Puls, Jurgen; Fischer, Wolfgang; **Haas, Rainer**

CORPORATE SOURCE: Max von Pettenkofer Institut fur Hygiene und Medizinische Mikrobiologie, LMU Munchen, Munchen,

SOURCE: D-80336, Germany  
Molecular Microbiology (2002), 43(4), 961-969  
CODEN: MOMIEE; ISSN: 0950-382X  
PUBLISHER: Blackwell Publishing Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB **Helicobacter pylori** type I strains harbor the cag pathogenicity island (cag-PAI), a 37 kb sequence, which encodes the components of a type IV secretion system. CagA, the first identified effector protein of the cag-PAI, is translocated into eukaryotic cells and tyrosine phosphorylated (CagAP-tyr) by a host cell tyrosine kinase. Translocation of CagA induces the dephosphorylation of a set of phosphorylated host cell proteins of unknown identity. CagA proteins of independent *H. pylori* strains vary in sequence and thus in the no. and compn. of putative tyrosine phosphorylation motifs (TPMs). The CagA protein of *H. pylori* strain J99 (CagAJ99) does not carry any of three putative tyrosine phosphorylation motifs (TPM-A, TPM-B or TPM-C) predicted by the MOTIF algorithm in CagA proteins. CagAJ99 is not tyrosine phosphorylated and is inactive in the dephosphorylation of host cell proteins. By site-specific mutagenesis, we introduced a TPM-C into CagAJ99 by replacing a single lysine with a tyrosine. This slight modification resulted in tyrosine phosphorylation of CagAJ99 and host cell protein dephosphorylation. In contrast, the removal of the indigenous TPM-C from CagAP12 did not abolish its tyrosine phosphorylation, suggesting that further phosphorylated sites are present in CagAP12. By generation of hybrid CagA proteins, a phosphorylation of the most N-terminal TPM-A could be excluded. Our data suggest that tyrosine phosphorylation at TPM-C is sufficient, but not exclusive, to activate translocated CagA. Activated CagAP-tyr might either convert into a phosphatase itself or activate a cellular phosphatase to dephosphorylate cellular phosphoproteins and modulate cellular signaling cascades of the host.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:584680 HCAPLUS  
DOCUMENT NUMBER: 136:196821  
TITLE: Natural transformation competence in  
**Helicobacter pylori** is mediated by the basic components of a type IV secretion system  
AUTHOR(S): Hofreuter, Dirk; Odenbreit, Stefan; Haas, Rainer  
CORPORATE SOURCE: Max von Pettenkofer Institut fur Hygiene und Medizinische Mikrobiologie, Munchen, D-80336, Germany  
SOURCE: Molecular Microbiology (2001), 41(2), 379-391  
CODEN: MOMIEE; ISSN: 0950-382X  
PUBLISHER: Blackwell Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB **Helicobacter pylori** (Hp), a Gram-neg. bacterial pathogen and etiol. agent of **gastroduodenal** disease in humans, is naturally competent for genetic transformation. Natural competence in bacteria is usually correlated with the presence of type IV pili or type IV pilin-like proteins, which are absent in Hp. Instead, we recently identified the



comB operon in Hp, carrying four genes tentatively designated as orf2, comB1, comB2 and comB3. We show here that all ComB proteins and the 37-amino-acid Orf2 peptide display significant primary sequence and structural homol./identity to the basic components of a type IV secretion app. ComB1, ComB2 and ComB3, now renamed ComB8, ComB9 and ComB10, correspond to the *Agrobacterium tumefaciens* VirB8, VirB9 and VirB10 proteins resp. The peptide Orf2 carries a lipoprotein motif and a second cysteine residue homologous to VirB7, and was thus designated ComB7. The putative ATPase ComB4, encoded by the open reading frame hp0017 of strain 26695, corresponds to virB4 of the *A. tumefaciens* type IV secretion system. A Hp comB4 transposon insertion mutant was totally defective in natural transformation. By complementation of a Hp .DELTA.comB deletion mutant, we demonstrate that each of the proteins from ComB8 to ComB10 is absolutely essential for the development of natural transformation competence. The putative lipoprotein ComB7 is not essential, but apparently stabilizes the app. and modulates the transformation efficiency. Thus, pathogenic type I Hp strains contain two functional independent type IV transport systems, one for protein translocation encoded by the cag pathogenicity island and one for uptake of DNA by natural transformation. The latter system indicates a possible novel mechanism for natural DNA transformation in bacteria.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:305032 HCAPLUS

DOCUMENT NUMBER: 135:225368

TITLE: Development of a *Helicobacter pylori* vaccine

AUTHOR(S): Banerjee, Subhas; Michetti, Pierre

CORPORATE SOURCE: Div. Gastroenterol., Beth Israel Deaconess med. Cent., Harvard Med. Sch., Boston, MA, USA

SOURCE: *Helicobacter pylori* (2001), 263-274. Editor(s): Achtman, Mark; Suerbaum, Sebastian. Horizon Scientific Press: Wymondham, UK.  
CODEN: 69AYWT

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review with 67 refs. Novel strategies are needed to control *H. pylori* infection on a global scale and the potential value of a vaccine is increasingly recognized. Studies in rodents have demonstrated the feasibility of prophylactic and therapeutic mucosal immunization against *Helicobacter* infections. Initial human trials showed that oral immunization with *H. pylori* urease is safe, immunogenic, and can result in a decreased gastric bacterial load. However, more potent vaccines will be needed to protect against or cure *H. pylori* infection in humans. To achieve this goal, our knowledge of the mechanisms of immune protection in the stomach needs to be improved. In rodents, the MHC II-restricted CD4+ T cell response plays a prominent role whereas antibodies are not necessary for protection. In humans, mechanisms that mediate protection against noninvasive gastric pathogens are largely unknown. Multivalent vaccines, safe adjuvants, and improved vaccine delivery systems all need to be studied. Divalent combinations of antigens are superior to single antigen vaccines in rodents. The availability of two genomic sequences of *H. pylori* will certainly help

identify addnl. candidate vaccine antigens. Detoxified bacterial toxin adjuvants, live vaccine vectors and alternate routes of immunization are currently being actively evaluated.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:116230 HCAPLUS

DOCUMENT NUMBER: 135:146510

TITLE: **Helicobacter pylori**, an adherent pain in the stomach

AUTHOR(S): Gerhard, Markus; Hirno, Siiri; Wadstrom, Torkel; Miller-Podraza, Halina; Teneberg, Susann; Karlsson, Karl-Anders; Appelmelk, Ben; Odenbreit, Stefan; Haas, Rainer; Arnqvist, Anna; Boren, Thomas

CORPORATE SOURCE: Department of Medicine II, Technical University of Munich, Munich, 81675, Germany

SOURCE: **Helicobacter pylori** (2001), 185-206. Editor(s): Achtman, Mark; Suerbaum, Sebastian. Horizon Scientific Press: Wymondham, UK. CODEN: 69AYWT

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review with many refs. Modern strains of **Helicobacter pylori** are the result of selection for life in the human **gastric** mucosa. This is a most demanding environment, with high acidity, peristalsis, **gastric** emptying and shedding of cells and mucus. In order to ensure efficient long-term survival and colonization, these microbes have developed arrays of adherence properties for homing to the optimal set of host cells. Survival demands an adequate balance between movement due to flagellar motility and attachment by adherence. This balance allows the microbes to take advantage of continuous supplies of nutrients without cutting off escape from the mucus layer to evade the cellular immune responses. *H. pylori* possesses a multitude of genetic mechanisms for the flexible shifting of adherence specificities to allow adaptation to the host and the local environment. The detailed characterization of the mechanisms that support and maintain bacterial adherence will identify key-elements for the persistence of infection that can be targeted for anti-microbial drug strategies.

L10 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:95344 HCAPLUS

DOCUMENT NUMBER: 134:263292

TITLE: Interaction of **Helicobacter pylori** with professional phagocytes: role of the cag pathogenicity island and translocation, phosphorylation and processing of CagA

AUTHOR(S): Odenbreit, Stefan; Gebert, Bettina; Puls, Jurgen; Fischer, Wolfgang; Haas, Rainer

CORPORATE SOURCE: Max von Pettenkofer Institut fur Hygiene und Medizinische Mikrobiologie, Munchen, D-80336, Germany

SOURCE: Cellular Microbiology (2001), 3(1), 21-31

CODEN: CEMIF5; ISSN: 1462-5814

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Chronic infection of the human **gastric** mucosa with **Helicobacter pylori** is a major cause of **gastroduodenal** pathologies, including peptic **ulcerations**, mucosa-assocd. lymphoid tissue (MALT) lymphoma and adenocarcinoma. **Helicobacter pylori** strains carrying the cag pathogenicity island, which encodes an active type IV protein secretion system (cag+ or type I strains), are preferentially assocd. with strong **gastric** inflammation and severe disease. We show here that cag+ H. pylori strains use the type IV secretion system to inject the bacterial protein CagA into various types of professional phagocytes, including human polymorphonuclear leukocytes (PMNs) and the human and murine macrophage cell lines THP-1 and J774A.1. CagA is rapidly tyrosine phosphorylated and proteolytically processed to generate a stable 35-45 kDa C-terminally tyrosine-phosphorylated protein fragment. H. pylori was efficiently ingested by the different types of phagocytic cells. A chromosomal deletion of the complete pathogenicity island had no significant effect on the rate of ingestion. Furthermore, the survival rate of H. pylori in the phagosome was unchanged between the wild type and a deletion mutant lacking the type IV secretion system. Thus, the type IV secretion system seems to be involved neither in active phagocytosis resistance nor in prolonged survival of the bacteria in phagocytic cells.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:555659 HCAPLUS

DOCUMENT NUMBER: 134:130191

TITLE: **Gastric** mucosal .alpha.4.beta.7-integrin-positive CD4 T lymphocytes and immune protection against **Helicobacter** infection in mice

AUTHOR(S): Michetti, Murielle; Kelly, Ciaran P.; **Kraehenbuhl, Jean-Pierre**; Bouzourene, Hanifa; **Michetti, Pierre**

CORPORATE SOURCE: Division of Gastroenterology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

SOURCE: Gastroenterology (2000), 119(1), 109-118  
 CODEN: GASTAB; ISSN: 0016-5085

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The integrin .alpha.4.beta.7 mediates homing of effector/memory lymphocytes to the intestine and the mucosa-assocd. lymphoid tissue. This study examd. the ability of .alpha.4.beta.7hi CD4+ T lymphocytes to home to the stomach and their role in immunization-mediated protection against **Helicobacter felis** infection. **Gastric** lamina propria and circulating mononucleated cells of naive, infected, and immunized Swiss Webster mice were isolated, and .alpha.4.beta.7-integrin expression was quantified by flow cytometry on CD4+ T lymphocytes. Anti-.alpha.4.beta.7-integrin antibody was used to block .alpha.4.beta.7 function in vivo. In naive mice, .alpha.4.beta.7hi CD4+ T cells were enriched approx. 10-fold in the **gastric** mucosa compared with

peripheral blood. Chronic *H. felis* infection did not alter these proportions, but oral immunization with *H. felis* sonicate plus cholera toxin (CT) or with CT alone markedly increased **gastric** .alpha.4.beta.7hi CD4+ T cells compared with naive and infected controls. Anti-.alpha.4.beta.7-integrin antibody blocked the protection induced by oral immunization with *H. felis* sonicate and CT. The integrin .alpha.4.beta.7 participates in the homing of CD4+ T lymphocytes to the stomach and in the protection of the **gastric** mucosa against *H. felis* infection.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:340294 HCAPLUS

DOCUMENT NUMBER: 134:111039

TITLE: Rapid and specific detection of **Helicobacter** pylori macrolide resistance in **gastric** tissue by fluorescent in situ hybridisation

AUTHOR(S): Trebesius, K.; Panthel, K.; Strobel, S.; Vogt, K.; Faller, G.; Kirchner, T.; Kist, M.; Heesemann, J.; Haas, R.

CORPORATE SOURCE: Max von Pettenkofer Institute for Hygiene and Medical Microbiology, Ludwig Maximilians, University Munich, Germany

SOURCE: Gut (2000), 46(5), 608-614  
CODEN: GUTTAK; ISSN: 0017-5749

PUBLISHER: BMJ Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background-The development of macrolide resistance in **Helicobacter** pylori is considered an essential reason for failure of antibiotic eradication therapies. The predominant mechanism of resistance to macrolides, particularly clarithromycin, is based on three defined mutations within 23S rRNA, resulting in decreased binding of the antibiotic to the bacterial ribosome. Aim-To develop an rRNA based whole cell hybridization method to detect **Helicobacter** species in situ within **gastric** tissue, simultaneously with its clarithromycin resistance genotype. Methods-A set of fluorescent labeled oligonucleotide probes was developed, binding either to *H pylori* 16S rRNA or 23S rRNA sequences contg. specific point mutations responsible for clarithromycin resistance. After hybridization and stringent washing procedures, labeling of intact single bacteria was monitored by fluorescence microscopy. The new approach was compared with PCR based assays, histol., and microbiol. culture. Results-In comparison with the phenotypic resistance measurement by E test, the genotypic clarithromycin resistance correlated perfectly (100%) for 35 *H pylori* isolates analyzed. In a set of **gastric** biopsy specimens (27) *H pylori* infection was confirmed by histol. (17/27) and correctly detected by whole cell hybridization. Five clarithromycin resistant strains were identified in **gastric** tissue specimens directly. Furthermore, non-cultivable coccoid forms of *H pylori* were easily detectable by whole cell hybridization. Conclusions-Whole cell hybridization of rRNA holds great promise for cultivation independent, reliable, and rapid (three hours) genotypic detn. of clarithromycin resistance in *H pylori*. Compared with

PCR techniques it is independent of nucleic acid preps., not prone to inhibition, and allows semiquant. visualisation of the bacteria within intact tissue samples.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:291921 HCAPLUS

DOCUMENT NUMBER: 132:288595

TITLE: The effect of ammonia on omeprazole-induced reduction of **gastric** acidity in subjects with **Helicobacter pylori** infection

AUTHOR(S): Bercik, Premysl; Verdu, Elena F.; Armstrong, David; Idstrom, Jan-Peter; Cederberg, Christer; Markert, Michele; Crabtree, Jean E.; Stolte, Manfred; **Blum, Andre L.**

CORPORATE SOURCE: Division of Gastroenterology and Central Laboratory of Clinical Chemistry, CHUV, Lausanne, Switz.

SOURCE: American Journal of Gastroenterology (2000), 95(4), 947-955

CODEN: AJGAAR; ISSN: 0002-9270

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Omeprazole produces a higher intragastric pH during **Helicobacter pylori** (H. pylori) infection than after cure. We tested the hypothesis that this difference is due to the prodn. of ammonia by H. pylori. **Gastric** acidity and acid output (AO) were measured overnight in 12 subjects, with and without omeprazole, before and 1 and 6 mo after cure of H. pylori infection. **Gastric** ammonia ([NH3]), total bile acid ([TBA]) and protein concns. and plasma omeprazole levels were measured. During omeprazole, median AO were 0.0 mmol/h before, 0.86 mmol/h (p = 0.003 vs before cure) at 1 mo, and 0.34 mmol/h (p = 0.02) at 6 mo after cure; median NH3 output was 0.17 mmol/h before, 0.03 mmol/h (p = 0.002) at 1 mo, and 0.02 mmol/h (p = 0.005) at 6 mo after cure. AO and NH3 output were similar 1 and 6 mo after cure. When cor. for [NH3], AO and **gastric** pH curves were similar before and after cure. Omeprazole plasma levels increased after cure and **gastric** [TBA] were unchanged. The higher pH obsd. before cure of H. pylori during omeprazole administration is attributable, in large part, to ammonia prodn. Other acid-neutralizing substances and changes in acid secretion may also be important, but duodenogastric reflex and omeprazole pharmacokinetics are not involved.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:228868 HCAPLUS

DOCUMENT NUMBER: 133:131032

TITLE: The effect of intra-**gastric** acidity and flora on the concentration of N-nitroso compounds in the stomach

AUTHOR(S): Viani, Francesco; Siegrist, Hans H.; Pignatelli, Brigitte; Cederberg, Christer; Idstrom, Jan-Peter;

Verdu, Elena F.; Fried, Michael; Blum, Andre  
L.; Armstrong, David  
CORPORATE SOURCE: Department of Gastroenterology, University Hospital,  
Lausanne, Switz.  
SOURCE: European Journal of Gastroenterology & Hepatology  
(2000), 12(2), 165-173  
CODEN: EJGHES; ISSN: 0954-691X  
PUBLISHER: Lippincott Williams & Wilkins  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Correa's hypothesis proposes that **gastric** carcinogenesis is due  
to atrophic **gastritis** and hypochlorhydria which permit  
**gastric** bacterial colonization, the redn. of dietary nitrates to  
nitrites and the formation of potentially carcinogenic N-nitroso compds.  
(NOCs). To test the hypothesis that omeprazole-induced hypochlorhydria is  
assocd. with increased intra-**gastric** concns. of nitrate-reducing  
bacteria (NRB), nitrites and NOCs, a single-blind study was conducted in  
healthy volunteers. The participants were 14 healthy subjects (seven  
female, mean age 24 yr), free of **Helicobacter pylori** infection,  
who received a one-week course of placebo followed by a two-week course of  
omeprazole, 20 mg daily. Fasted **gastric** samples, aspirated  
using a sterile double-lumen nasogastric tube at the end of the 1st week  
(placebo) and the 2nd and 3rd weeks (omeprazole), were cultured  
aerobically and anaerobically; **gastric** pH and intra-  
**gastric** concns. of nitrates, nitrites and NOCs were also detd.  
After weeks 1, 2 and 3, the intra-**gastric** concns. of  
nitrate-reducing bacteria exceeded 105 colony-forming units (c.f.u.)/mL in  
3, 7 and 9 subjects, resp. A **gastric** pH >4.0 was assocd. with  
increased NRB; however, neither increased **gastric** pH nor  
increased NRB, alone or in combination, was assocd. with increased intra-  
**gastric** concns. of nitrites or NOCs. A two-week increase in  
**gastric** pH in healthy, H. pylori-neg. subjects was assocd. with  
increased intra-**gastric** concns. of nitrate-reducing bacteria but  
not of nitrites or N-nitroso compds. These data suggest that reduced  
**gastric** acid secretion is not a necessary precursor to the  
formation of carcinogenic N-nitroso compds. and that other mechanisms  
should be invoked to explain **gastric** carcinogenesis.  
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:149963 HCAPLUS

DOCUMENT NUMBER: 132:277466

TITLE: Translocation of **Helicobacter pylori** CagA  
into **gastric** epithelial cells by type IV  
secretion

AUTHOR(S): Odenbreit, Stefan; Pills, Jurgen; Sedimaier, Bettina;  
Gerland, Elke; Fischer, Wolfgang; Haas, Rainer

CORPORATE SOURCE: Max von Pettenkofer Inst. Hygiene and Med.  
Microbiology, Ludwig-Maximilians Univ. Munich, Munich,  
D-80336, Germany

SOURCE: Science (Washington, D. C.) (2000), 287(5457),  
1497-1500  
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The Gram-neg. bacterium **Helicobacter pylori** is a causative agent of **gastritis** and peptic ulcer disease in humans. Strains producing the CagA antigen (cagA+) induce strong **gastric** inflammation and are strongly assocd. with **gastric** adenocarcinoma and MALT Lymphoma. We show here that such strains translocate the bacterial protein CagA into **gastric** epithelial cells by a type IV secretion system, encoded by the cag pathogenicity island. CagA is tyrosine-phosphorylated and induces changes in the tyrosine phosphorylation state of distinct cellular proteins. Modulation of host cells by bacterial protein translocation adds a new dimension to the chronic **Helicobacter** infection with yet unknown consequences.

L10 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:108369 HCAPLUS

DOCUMENT NUMBER: 132:249351

TITLE: **Helicobacter pylori** activates the histidine decarboxylase promoter through a mitogen-activated protein kinase pathway independent of pathogenicity island-encoded virulence factors

AUTHOR(S): Wessler, Silja; Hocker, Michael; Fischer, Wolfgang; Wang, Timothy C.; Rosewicz, Stefan; Haas, Rainer; Wiedenmann, Bertram; Meyer, Thomas F.; Naumann, Michael

CORPORATE SOURCE: Max-Planck-Institut fur Infektionsbiologie, Abteilung Molekulare Biologie, Berlin, Germany

SOURCE: Journal of Biological Chemistry (2000), 275(5), 3629-3636

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Helicobacter pylori** infection of the **gastric** mucosa is accompanied by an activated histamine metab. Histamine plays a central role in the regulation of **gastric** acid secretion and is involved in the pathogenesis of **gastroduodenal ulcerations**. Histidine decarboxylase (HDC) is the rate-limiting enzyme for histamine prodn., and its activity is regulated through transcriptional mechanisms. The present study investigated the effect of H. pylori infection on the transcriptional activity of the human HDC (hHDC) promoter in a **gastric** epithelial cell line (AGS) and analyzed the underlying mol. mechanisms. Our studies demonstrate that H. pylori infection potently transactivated the hHDC promoter. The H. pylori-responsive element of the hHDC gene was mapped to the sequence +1 to +27 base pairs, which shows no homol. to known cis-acting elements and also functions as a **gastrin**-responsive element. H. pylori regulates the activity of this element via a Raf-1/MEK/ERK pathway, which was activated in a Ras-independent manner. Furthermore, we found that H. pylori-induced transactivation of the hHDC promoter was independent of the cag pathogenicity island and the vacuolating cytotoxin A gene and therefore

may be exerted through (a) new virulence factor(s). A better understanding of *H. pylori*-directed hHDC transcription can provide novel insights into the mol. mechanisms of *H. pylori*-dependent gene regulation in **gastric** epithelial cells and may lead to new therapeutic approaches.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:764237 HCAPLUS

DOCUMENT NUMBER: 132:20800

TITLE: Determination of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

INVENTOR(S): Haas, Rainer; Trebesius, Karlheinz; Apfel, Heiko

PATENT ASSIGNEE(S): Creatogen Biosciences G.m.b.H., Germany

SOURCE: PCT Int. Appl., 84 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961660	A1	19991202	WO 1999-EP3527	19990521
W:		AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
DE 19916610	A1	19991125	DE 1999-19916610	19990413
CA 2329057	AA	19991202	CA 1999-2329057	19990521
AU 9942658	A1	19991213	AU 1999-42658	19990521
BR 9910646	A	20010130	BR 1999-10646	19990521
EP 1078104	A1	20010228	EP 1999-938039	19990521
R:		AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE		
JP 2002516665	T2	20020611	JP 2000-551040	19990521
PRIORITY APPLN. INFO.:			DE 1998-19823098 A	19980522
			DE 1999-19916610 A	19990413
			WO 1999-EP3527 W	19990521

AB The invention concerns the detn. of bacterial antibiotic resistance by in situ hybridization using a combination of at least two mutation-specific 23S rRNA-targeted oligonucleotide probes, along with probes that are targeted to *E. coli* homologous regions of *Helicobacter pylori* 16S rRNA. Probes are fluorescent or enzyme labeled; samples are tissues or body fluids; microorganisms are isolated; detected without culturing or cultured; cell walls are made permeable; and nucleic acids are isolated



for in situ hybridization. Fluorescence microscopy is used for detection. **Helicobacter** species, Mycobacteria, Chlamydia, etc. can be identified and the antibiotic resistance detd. by the method. Resistance to macrolides, lincosamide, aminoglycosides, aminocyclitol, tetracycline and chloramphenicol can be detected. The invention also concerns a test kit contg. the necessary reagents and probes.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:717013 HCAPLUS  
DOCUMENT NUMBER: 132:48418  
TITLE: Activation of activator protein 1 and stress response kinases in epithelial cells colonized by **Helicobacter pylori** encoding the cag pathogenicity island  
AUTHOR(S): Naumann, Michael; Wessler, Silja; Bartsch, Cornelia; Wieland, Bjorn; Covacci, Antonello; Haas, Rainer; Meyer, Thomas F.  
CORPORATE SOURCE: Max-Planck-Institut fur Infektionsbiologie, Abteilung Molekulare Biologie, Berlin, 10117, Germany  
SOURCE: Journal of Biological Chemistry (1999), 274(44), 31655-31662  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB **Helicobacter pylori** interacts with the apical membrane of the gastric epithelium and induces a no. of proinflammatory cytokines/chemokines. The subsequent infiltration of macrophages and granulocytes into the mucosa leads to gastric inflammation accompanied by epithelial degeneration. Gastric diseases, e.g. peptic ulcer or gastric adenocarcinoma, are more common among people infected with H. pylori strains producing VacA (vacuolating cytotoxin A) and possessing a cag (cytotoxin-assocd. antigen A) pathogenicity island. For the induction of the cytokine/chemokine genes in response to H. pylori, we studied the signaling leading to the nuclear activation of the early response transcription factor activator protein 1 (AP-1). We found that H. pylori strains carrying the pathogenicity island induce activation of AP-1 and nuclear factor .kappa.B. In contrast to the wild type or an isogenic strain without the vacA gene, isogenic H. pylori strains with mutations in certain cag genes revealed only weak AP-1 and nuclear factor .kappa.B activation. In respect to the mol. components that direct AP-1 activity, our results indicate a cascade of the cellular stress response kinases c-Jun N-terminal kinase, MAP kinase kinase 4, and p21-activated kinase, and small Rho-GTPases including Rac1 and Cdc42, which contributes to the activation of proinflammatory cytokines/chemokines induced by H. pylori encoding the cag pathogenicity island.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:709918 HCAPLUS  
 DOCUMENT NUMBER: 132:34431  
 TITLE: Urease-based mucosal immunization against **Helicobacter** heilmannii infection induces corpus atrophy in mice  
 AUTHOR(S): Dieterich, Christine; Bouzourene, Hanifa; Blum, Andre L.; Cortesy-Theulaz, Irene E.  
 CORPORATE SOURCE: Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, CH-1011, Switz.  
 SOURCE: Infection and Immunity (1999), 67(11), 6206-6209  
 CODEN: INFIBR; ISSN: 0019-9567  
 PUBLISHER: American Society for Microbiology  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Mucosal immunization with **Helicobacter** heilmannii urease B or H. pylori urease, given nasally with cholera toxin, protects BALB/c mice against H. heilmannii infection and reduces a preexisting infection. However, immunization aggravates gastric corpus atrophy. The authors' results underline the necessity of defining immunization regimens that do not enhance mucosal damage.  
 REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:428883 HCAPLUS  
 DOCUMENT NUMBER: 131:210809  
 TITLE: New inhibitors of **Helicobacter** pylori urease holoenzyme selected from phage-displayed peptide libraries  
 AUTHOR(S): Houimel, Mehdi; Mach, Jean-Pierre; Cortesy-Theulaz, Irene; Cortesy, Blaise; Fisch, Igor  
 CORPORATE SOURCE: Institute of Biochemistry, University of Lausanne, Epalinges, 1066, Switz.  
 SOURCE: European Journal of Biochemistry (1999), 262(3), 774-780  
 CODEN: EJBCAI; ISSN: 0014-2956  
 PUBLISHER: Blackwell Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Urease is an important virulence factor for **Helicobacter** pylori and is crit. for bacterial colonization of the human gastric mucosa. Specific inhibition of urease activity has been proposed as a possible strategy to fight this bacteria which infects billions of individual throughout the world and can lead to severe pathol. conditions in a limited no. of cases. We have selected peptides which specifically bind and inhibit H. pylori urease from libraries of random peptides displayed on filamentous phage in the context of pIII coat protein. Screening of a highly diverse 25-mer combinatorial library and two newly constructed random 6-mer peptide libraries on solid phase H. pylori urease holoenzyme allowed the identification of two peptides, 24-mer TFLPQPRCSALLRYLSEGDGVIVPS and 6-mer YDFYWW that can bind and inhibit the activity of urease purified from H. pylori. These two peptides were chem. synthesized and their inhibition consts. (Ki) were found to be 47 .mu.M

for the 24-mer and 30 .mu.M for the 6-mer peptide. Both peptides specifically inhibited the activity of H. pylori urease but not that of Bacillus pasteurii.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:346011 HCAPLUS

DOCUMENT NUMBER: 131:17350

TITLE: Effect of whey-based culture supernatant of Lactobacillus acidophilus (johnsonii) Lal on Helicobacter pylori infection in humans

AUTHOR(S): Michetti, Pierre; Dorta, G.; Wiesel, P. H.; Brassart, D.; Verdu, E.; Herranz, M.; Felley, C.; Porta, N.; Rouvet, M.; Blum, A. L.; Cortesy-Theulaz, I.

CORPORATE SOURCE: Division Gastroenterology, Department Medicine, Univ. Lausanne, Lausanne, Switz.

SOURCE: Digestion (1999), 60(3), 203-209  
CODEN: DIGEBW; ISSN: 0012-2823

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Specific strains of L. acidophilus are known to inhibit intestinal cell adhesion and invasion by enterovirulent bacteria. As L. acidophilus can survive transiently in the human stomach, it may down-regulate H. pylori infection. The ability of L. acidophilus (johnsonii) Lal supernatant to interfere with H. pylori bacterial growth, urease activity, and adhesion to epithelial cells was tested in vitro. Its effect on H. pylori infection in volunteers was monitored in a randomized, double-blind, controlled clin. trial, using a drinkable, whey-based, Lal culture supernatant. H. pylori infected volunteers were treated 14 days with 50 mL of Lal supernatant 4 .times. a day combined with either omeprazole 20 mg 4 .times. a day or with placebo. Infection was assessed by breath test, endoscopy, and biopsy sampling, performed at inclusion, immediately at the end of the treatment (breath test only), and 4 wk after the end of the treatment. Lal supernatant inhibited H. pylori growth in vitro, regardless of previous binding of H. pylori to epithelial cells. In 20 subjects (8 females, 12 males, mean age 33.1 yr) a marked decrease in breath test values was obsd. immediately after treatment with Lal supernatant, both in the omeprazole and in the placebo group (median 12.3 vs. 28.8 and 9.4 vs. 20.4, resp.). In both treatment groups, breath test values remained low 6 wk after treatment (omeprazole treated 19.2, placebo treated 8.3; vs. pretreatment), but the persistence of H. pylori infection was confirmed in gastric biopsies. Lal culture supernatant shown to be effective in vitro has a partial, acid-independent long-term suppressive effect on H. pylori in humans.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:210574 HCAPLUS

DOCUMENT NUMBER: 131:16185

TITLE: Genetic and functional characterization of the alpAB

gene locus essential for the adhesion of  
**Helicobacter pylori** to human **gastric**  
tissue

AUTHOR(S): Odenbreit, Stefan; Till, Markus; Hofreuter, Dirk;  
Faller, Gerhard; **Haas, Rainer**

CORPORATE SOURCE: Max-Planck-Institut fur Biologie, Tübingen, D-72076,  
Germany

SOURCE: Molecular Microbiology (1999), 31(5), 1537-1548  
CODEN: MOMIEE; ISSN: 0950-382X

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this study, we isolated and characterized a chromosomal locus of  
**Helicobacter pylori** previously identified by transposon shuttle  
mutagenesis as being involved in the adhesion of the pathogen to  
**gastric** epithelial cells. Two closely homologous genes were  
identified, designated as alpA and alpB, encoding outer membrane (OM)  
proteins of 518 amino acids each. They are members of the outer membrane  
protein supergene family identified in the H. pylori 26695 complete genome  
sequence. AlpA carries a functional lipoprotein signal sequence. AlpB  
carries a putative std. N-terminal signal sequence and shows a strong  
amino-acid sequence identity to AlpA. Transposon insertion mutagenesis,  
immunoblotting and primer extension studies indicate that both genes are  
organized in an operon, but no obvious consensus promoter sequence was  
found upstream of the transcriptional start site. The C-terminal portion  
of both proteins is predicted to form a porin-like .beta.-barrel in the  
outer membrane, consisting of 14 transmembrane amphipathic P-strands.  
Adhesion expts. with defined isogenic mutants indicate that both proteins  
are necessary for specific adherence of H. pylori to human **gastric**  
tissue. The pattern of AlpAB-dependent adherence of H. pylori to the  
**gastric** epithelial surface shows a clear difference to the  
BabA2-mediated adherence to Lewis, suggesting that a different receptor is  
involved.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:149566 HCAPLUS

DOCUMENT NUMBER: 131:13722

TITLE: Effects of pumaprazole (BY841), a novel reversible  
proton pump antagonist, and of omeprazole, on  
intra gastric acidity before and after cure of  
**Helicobacter pylori** infection

AUTHOR(S): Martinek, J.; **Blum, A. L.**; Stolte, M.;  
Hartmann, M.; Verdu, E. F.; Luhmann, R.; Dorta, G.;  
Wiesel, P.

CORPORATE SOURCE: Division of Gastroenterology, CHUV, Lausanne, Switz.

SOURCE: Alimentary Pharmacology and Therapeutics (1999),  
13(1), 27-34  
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Omeprazole produces a higher intra gastric pH in the presence of

**Helicobacter pylori** infection than after cure. To investigate whether this effect also occurs with pumaprazole (BY841), a reversible proton pump antagonist which, in contrast to omeprazole, does not require activation in the acid compartment of the parietal cell. In a randomized, crossover, double-blind study. 24-H intragastric pH was measured in 13 H. pylori-pos. subjects before and after a 1-wk course of omeprazole (20 mg o.d.) or of pumaprazole (100 mg b.d.). The studies were repeated after the infection was cured. In the absence of drug administration, the median 24-h pH values before cure (median 2.0, 90% CI: 1.2-3.2) did not differ from those after cure (median 1.5, 90% CI: 1.3-2.2; P = 0.115). The 24-h pH values were higher before cure of the infection than after during both pumaprazole (6.0, 4.8-6.7 vs. 4.3, 2.6-5.7; P = 0.002) and omeprazole (5.8, 4.0-6.2 vs. 3.6, 2.8-5; P = 0.004). Both before and after cure, there were no significant differences between the two drugs with respect to acid inhibition over the 24-h period. The median decrease in acid inhibition after cure of the infection (calcd. as the difference in H<sup>+</sup> activity in mmol/L) during pumaprazole (median 0.05, 90% CI: 6.times.10-4-2.3) was no different from that during omeprazole (median 0.2, 90% CI: 3.times.10-3-1.5; P = 0.6). Both before and after cure of H. pylori infection, pumaprazole raised the intragastric pH over a 24-h period to a similar degree as omeprazole. H. pylori infection similarly augments the pH-increasing effect of both drugs. This effect is related to H. pylori infection and not to an increased activation of acid inhibitory agents in the parietal cell compartment.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:664234 HCAPLUS

DOCUMENT NUMBER: 130:106751

TITLE: Properties and function of the P type ion pumps cloned from **Helicobacter pylori**

AUTHOR(S): Melchers, Klaus; Herrmann, Lutz; Mauch, Frieder; Bayle, Denis; Heuermann, Dorothee; Weitzenegger, Thomas; Schuhmacher, Alexander; Sachs, George; Haas, Rainer; Bode, Gunter; Bensch, Klaus; Schafer, Klaus P.

CORPORATE SOURCE: Department of Molecular Biology, Byk Gulden Pharmaceuticals, Konstanz, 78462, Germany

SOURCE: Acta Physiologica Scandinavica, Supplementum (1998), 163(643), 123-135

CODEN: APSSAD; ISSN: 0302-2994

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three distinct P type pumps were cloned from H. pylori 69A. Two of these pumps, ATPase 439 and ATPase 948 (CopA), were isolated by gene library screening using DNA oligonucleotide primers. Amino acid similarities found for the predicted proteins were about 50% to Cd<sup>2+</sup>/Cu<sup>2+</sup> pumps. Gene disruption mutagenesis rendered the H. pylori knockout mutants more sensitive to Zn<sup>2+</sup> and Cd<sup>2+</sup> (ATPase 439) or Cu<sup>2+</sup> (CopA). Some of the ATPase 439-deficient mutants were neg. for urease activity while the majority of the mutants remained pos. Functional diversity of the pumps was also reflected by the ion affinities found for N-terminal peptides of

CopA to Cu<sup>2+</sup> and of ATPase 439 to Ni<sup>2+</sup>, Cu<sup>2+</sup> and Co<sup>2+</sup>. The membrane domain of the two pumps were exptl. shown to consist of eight membrane spans. When ATPase 439 was expressed under control of a tac promoter in *Escherichia coli*, vanadate-sensitive phosphate accumulation was obsd. cytochem. along the membrane of the host cells. The third P type pump (ATPase 115) which also exhibited homol. to transition metal ATPase was identified by sequencing a library of *H. pylori* membrane genes. The hydropathy plot of this pump was very similar to the former *H. pylori* ATPases, whereas the N-terminal ion binding region was distinct. It was concluded that, in *H. pylori*, the presence of three transition metal ATPases with distinct ion specificity contributes to the adaptive mechanisms for **gastric** survival.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:380151 HCAPLUS

DOCUMENT NUMBER: 129:131899

TITLE: Natural competence for DNA transformation in

**Helicobacter pylori**: identification and genetic characterization of the comB locus

AUTHOR(S): Hofreuter, Dirk; Odenbreit, Stefan; Henke, Gabriele;

**Haas, Rainer**

CORPORATE SOURCE: Infektionsbiologie, Max-Planck-Institut for Biologie, Tübingen, D-72076, Germany

SOURCE: Molecular Microbiology (1998), 28(5), 1027-1038

CODEN: MOMIEE; ISSN: 0950-382X

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The Gram-neg. bacterial pathogen **Helicobacter pylori**, an important etiol. agent of **gastroduodenal** disease in humans, belongs to a group of bacterial species displaying competence for genetic transformation. Here, the authors describe the comB gene locus of *H. pylori* involved in DNA transformation competence. It consists of a cluster of four tandemly arranged genes with partially overlapping open reading frames, orf2, comB1, comB2 and comB3, constituting a single transcriptional unit. Orf2 encodes a 37-amino-acid peptide carrying a signal sequence, whereas comB1, comB2 and comB3 produce 29kDa, 38kDa and 42kDa proteins, resp., as demonstrated by immunoblotting with specific antisera. For Orf2 and ComB1, no homologous proteins were identified in the database. For ComB3, the best homologies were found with TraS/TraB from the *Pseudomonas aeruginosa* conjugative plasmid RP1 and Trb1 of plasmid RP4, VirB10 from the Ti plasmid of *Agrobacterium tumefaciens* and PtIG, a protein involved in secretion of pertussis toxin of *Bordetella pertussis*. Defined transposon knock-out mutants in individual comB genes resulted in transformation-defective phenotypes ranging from a 90% redn. to a complete loss of the natural transformation efficiency. The comB2 and comB3 genes show homol. to HP0528 and HP0527, resp., located on the cagII pathogenicity island of *H. pylori* strain 26695.

L10 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:281567 HCAPLUS

DOCUMENT NUMBER: 129:91101

TITLE: Presence of multiple "**Helicobacter** heilmannii" strains in an individual suffering from **ulcers** and in his two cats

AUTHOR(S): Dieterich, Christine; Wiesel, Paul; Neiger, Reto; **Blum, Andre; Corthesy-Theulaz, Irene**

CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, CH-1011, Switz.

SOURCE: Journal of Clinical Microbiology (1998), 36(5), 1366-1370  
CODEN: JCMIDW; ISSN: 0095-1137

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Circumstantial evidence suggests that "**Helicobacter** heilmannii" infection is an example of zoonosis. The presence of "H. heilmannii" strains in a human subject with acute **gastric** erosions, in his two cats, and in two unrelated cats was analyzed, and the genetic relatedness of the human and feline strains was assessed. A 580-bp, PCR-amplified sequence of "H. heilmannii" urease B gene (ureB) obtained from biopsies from the human subject and his two cats was restricted with AluI and cloned for sequencing. Anal. of the restriction fragment length polymorphism of the ureB-amplified product suggested the presence of different individual "H. heilmannii" strains in the cats and of three distinct strains in the human subject. One of the "H. heilmannii" ureB sequences amplified from the human subject's biopsies was identical to that derived from one of his cats. The degree of similarity between the other "H. heilmannii" human and feline nucleotide sequences was higher than 97%. Most of the base substitutions were conservative. We conclude that human and animal "H. heilmannii" strains are closely related and that humans can be infected by more than one "H. heilmannii" strain, as has been obsd. for **Helicobacter** pylori.

L10 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:2613 HCAPLUS

DOCUMENT NUMBER: 128:56914

TITLE: **Gastroenterology**. Part 2. Acid research and **ulcer** therapy

AUTHOR(S): Martinek, Jan; Koelz, Hans Rudolf; **Blum, Andre L.**

CORPORATE SOURCE: Division Gastro-Enterologie, Centre Hospitalier, Universitaire Vaudois, Lausanne, CH-1011, Switz.

SOURCE: Arzneimittel-Forschung (1997), 47(12), 1424-1435  
CODEN: ARZNAD; ISSN: 0004-4172

PUBLISHER: Editio Cantor Verlag

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB Three discoveries of the last thirty years have revolutionized acid research and **ulcer** therapy: H<sub>2</sub>-receptors and their competitive inhibition, the acid pump and its blockade and, finally, **Helicobacter** pylori and its central role in **ulcer** disease. Today the problem of **ulcer** treatment is more or less solved by the correct use of antibiotics, while the cure of reflux disease is still problematic: pump blockers accelerate the healing of mucosal

breaks and prevent, when given at long term, recurrences but they cannot change the natural history of reflux disease. These facts form the basis for future research. This article is reviewed by 112 refs.

L10 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:684504 HCAPLUS

DOCUMENT NUMBER: 127:356945

TITLE: Polyhydroxybutrate biosynthetic enzymes of **Helicobacter** for use as targets in the diagnosis and treatment of **gastrointestinal** disease

INVENTOR(S): **Corthesy-Theulaz, Irene**

PATENT ASSIGNEE(S): Kieta Holdings S.A., Switz.; Corthesy-Theulaz, Irene

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9738110	A2	19971016	WO 1997-IB409	19970403
W:		AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		
AU 9723040	A1	19971029	AU 1997-23040	19970403
EP 904381	A2	19990331	EP 1997-915631	19970403
R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		
US 6060241	A	20000509	US 1997-834776	19970403
PRIORITY APPLN. INFO.:			US 1996-14906P	P 19960405
			WO 1997-IB409	W 19970403
AB			A poly-3-hydroxybutyrate metabolic pathway essential for <b>Helicobacter pylori</b> survival in a host is described for use as a target in the diagnosis and treatment of infection. A novel CoA transferase ((Hp)CoA-t), thiolase and PHB synthase are described and genes encoding the (Hp) CoA-t and thiolase are cloned and methods for detecting the genes and the enzymes are described. Methods for the detn. of a propensity to develop <b>gastritis</b> , peptic <b>ulcer</b> disease, or <b>gastric</b> cancer is provided for by detection methods. Methods are also provided for the use of (Hp) CoA-t, thiolase or PHB synthase proteins and fragments retaining enzymic activity in the identification of potential drug candidates for the treatment of some types of <b>gastric</b> disease. Pharmaceutical compns. contg. (Hp) CoA-t protein fragments, antisense nucleic acids or other inhibitors of (Hp) CoA-t, thiolase and PHB synthase as well as methods for their use in the treatment of some types of <b>gastric</b> disease are also provided. Cloning and expression of the genes in <i>Escherichia coli</i> is described. H.	



pylori mutants lacking one of the subunits of the CoA transferase were constructed by std. methods were unable to colonize germ-free BALB/c mice.

L10 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:560101 HCAPLUS  
 DOCUMENT NUMBER: 127:229261  
 TITLE: Effect of curing **Helicobacter pylori** infection on intragastric acidity during treatment with ranitidine in patients with duodenal **ulcer**  
 AUTHOR(S): Labenz, J.; Tillenburg, B.; Peitz, U.; Verdu, E.; Stolte, M.; Borsch, G.; **Blum, A. L.**  
 CORPORATE SOURCE: Department of Internal Medicine and Gastroenterology, Elisabeth Hospital, Essen, D-45138, Germany  
 SOURCE: Gut (1997), 41(1), 33-36  
 CODEN: GUTTAK; ISSN: 0017-5749  
 PUBLISHER: BMJ Publishing Group  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB In patients with duodenal **ulcer** cure of **Helicobacter pylori** infection resulted in a pronounced decrease in intragastric pH during treatment with omeprazole. Our aim was to test the hypothesis that treatment of H pylori adversely affects the pH response to ranitidine. Eighteen patients with duodenal **ulcer** who were infected with H pylori were studied. Twenty four hour pH recordings were performed during treatment with ranitidine (300 mg) at night before and four to six weeks after cure of H pylori infection. Presence of H pylori was assessed by a rapid urease test, culture, histol., and a 13C urea breath test. Also, the fasting **gastrin** concns. were measured before and after treatment for H pylori infection. Cure of H pylori infection resulted in a considerable improvement in both antral and corpus **gastritis** and a decrease in fasting **gastrin** concns. As a result of the cure the night time intragastric pH during treatment with ranitidine decreased (median pH 6.8 .nu. 5.4; p=0.007), whereas the acidity during the daytime was not affected. In patients with duodenal **ulcer** the intragastric pH during treatment with ranitidine depends on H pylori. However, the loss of effectiveness in altering pH seems to be less pronounced than previously found with omeprazole.

L10 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:325719 HCAPLUS  
 DOCUMENT NUMBER: 127:48538  
 TITLE: MALT-type lymphoma of the stomach is associated with **Helicobacter pylori** strains expressing the CagA protein  
 AUTHOR(S): Eck, Matthias; Schmauer, Bernd; **Haas, Rainer**; Greiner, Axel; Czub, Stefanie; Mueller-Hermelink, Hans Konrad  
 CORPORATE SOURCE: Institut fur Pathologie, Universitat Wurzburg, Wurzburg, Germany  
 SOURCE: Gastroenterology (1997), 112(5), 1482-1486  
 CODEN: GASTAB; ISSN: 0016-5085  
 PUBLISHER: Saunders  
 DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Helicobacter pylori** is considered to be involved in the pathogenesis of **gastric** lymphoma of mucosa-assocd. lymphoid tissue (MALT) type. Strains expressing the CagA protein (CagA+ strains) have been strongly assocd. with severe **gastritis**, duodenal **ulceration**, and **gastric** adenocarcinoma. The aim of this study was to det. the presence of *H. pylori* as well as incidence of CagA+ strains in **gastric** MALT-type lymphoma. Sera of 68 patients with **gastric** MALT-type lymphoma (22 with low grade, 36 with high grade, and 10 with secondary high grade) were obtained, and the serol. response to CagA was studied by immunoblotting using a purified recombinant CagA protein, a CagA+ strain, and the corresponding isogenic CagA- mutant. Of the patients with MALT-type lymphoma, 98.5% (67 of 68 patients) were *H. pylori* seropos. In the only seroneg. patient, the bacterium was detected histol. by Warthin-Starry staining. Of the seropos. patients, 95.5% had serum IgG antibodies to CagA compared with 67% of an *H. pylori*-pos. control group (33 of 49 patients;  $P = 0.000037$ ) with chronic active **gastritis**. These results indicate infection of almost all patients with MALT-type lymphoma by CagA+ *H. pylori* strains. Strains expressing the CagA protein seem to play a crucial role in the pathogenesis of **gastric** MALT-type lymphoma.

L10 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:317123 HCAPLUS

DOCUMENT NUMBER: 126:338649

TITLE: Efficacy of omeprazole one year after cure of **Helicobacter pylori** infection in duodenal **ulcer** patients

AUTHOR(S): Labenz, Joachim; Tillenbourg, Birgit; Peitz, Ulrich; Boersch, Gereon; Idstroem, Jan-Peter; Verdu, Elena; Stolte, Manfred; **Blum, Andre L.**

CORPORATE SOURCE: Department of Internal Medicine and Gastroenterology, Elisabeth Hospital Essen, Germany

SOURCE: American Journal of Gastroenterology (1997), 92(4), 576-581

CODEN: AJGAAR; ISSN: 0002-9270

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have previously shown that, in duodenal **ulcer** patients, pH control by omeprazole is less pronounced after cure of **Helicobacter pylori** infection. The present study was designed to test the hypothesis that this response to omeprazole persists 1 yr after cure of *H. pylori* infection. In 12 duodenal **ulcer** patients, intragastric acidity was measured with a glass electrode during treatment with omeprazole (20 mg) once daily before, and 4-6 wk and 1 yr after, cure of *H. pylori* infection. *H. pylori* infection was assessed by [<sup>13</sup>C]urea breath test, culture, histol. (Warthin Starry stain), and rapid urease test. Cure of *H. pylori* infection resulted in a lowered pH during omeprazole treatment. This effect persisted after 1 yr. Median 24-h **gastric** pH before *H. pylori* treatment was 5.6; 4-6 wk after cure of the infection it was 2.9 ( $p = 0.003$ ), and 1 yr after cure of the infection it remained unchanged (pH = 2.5;  $p = 0.5$ ). Accordingly, twice as much time was spent above pH 3 and pH 4 before *H. pylori* treatment than

1 or 12 mo after cure (percent of time .gtoreq. pH 3: 82.7 vs. 49.7 vs. 43.1; percent of time .gtoreq. pH 4: 72.7 vs. 38.3 vs. 26.4). In duodenal **ulcer** patients, cure of *H. pylori* infection resulted in a marked rapid and persistent decrease of the pH increasing effect of omeprazole. Therefore, *H. pylori* is a determinant of the pH achieved in response to omeprazole treatment in duodenal **ulcer** patients.

L10 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:274424 HCAPLUS

DOCUMENT NUMBER: 126:342542

TITLE: The selection of dairy bacterial strains with probiotic properties based on their adhesion to human intestinal epithelial cells

AUTHOR(S): Brassart, D.; Neeser, J.-R.; Michetti, P.; Servin, A. L.

CORPORATE SOURCE: Nestle Research Center, Lausanne, Switz.

SOURCE: Bacteries Lactiques, Actes du Colloque LACTIC 94, Caen, Fr., Sept. 7-9, 1994 (1995), Meeting Date 1994, 201-212. Editor(s): Novel, Georges; Le Querler, Jean-Francois. Presses Universitaires de Caen: Caen, Fr.

CODEN: 64HMA5

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB Lactic acid bacteria (LAB), in certain fermented milks, survive intestinal transit in the human and exert beneficial biol. effects (probiotic effects) therein. Since such bacteria does not permanently colonize the human intestine, it is desirable to select strains better adapted to this ecosystem. Adhesion to human intestinal epithelial cells is a criteria worthy of consideration. The use of the differentiated human intestinal epithelial cell lines, HT-29 and Caco-2, in the selection of adherent human strains from the Nestec collection was reported. Adhesion, although not a general feature of LAB seems mediated, at least with respect to *Lb. acidophilus* LA1 and three bifidobacterial strains (Bbr4, B116, B11), through adhesion-promoting protein(s). Also, LA1 significantly inhibits cell adhesion and/or cell invasion by pathogenic *Escherichia coli*, *Salmonella typhimurium*, or *Yersinia pseudotuberculosis*. In addn., LA1 similarly affects *Helicobacter pylori*, the **ulcer** assocd. bacterium. Comparable results were obtained with adherent human bifidobacteria. All this was discussed with 20 refs.

L10 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:23697 HCAPLUS

DOCUMENT NUMBER: 126:69765

TITLE: Intragastric pH during treatment with omeprazole: Role of *Helicobacter pylori* and *H. pylori*-associated **gastritis**

AUTHOR(S): Verdu, E. F.; Armstrong, D.; Idstrom, J.-P.; Labenz, J.; Stolte, M.; Borsch, G.; Blum, A. L.

CORPORATE SOURCE: Division Gastroenterology, CHUV, Lausanne, Switz.

SOURCE: Scandinavian Journal of Gastroenterology (1996), 31(12), 1151-1156

CODEN: SJGRA4; ISSN: 0036-5521

PUBLISHER: Scandinavian University Press

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Omeprazole treatment produces lower intragastric pH values 4 wk after cure of **Helicobacter pylori** infection than before. The authors therefore investigated the effect of healing H. pylori-assocd. **gastritis** on intragastric pH in the presence and in the absence of omeprazole therapy. Before and on day 8 of omeprazole, 20 mg once daily, 24-h intragastric pH-recordings were performed in 14 subjects with H. pylori infection and repeated 4 and 52 wk after cure of infection. **Gastritis** severity in corpus and antrum was graded by using a modified Sydney system. In the absence of omeprazole administration, median 24-h pH values before cure did not differ from those 4 and 52 wk after cure. On day 8 of omeprazole administration, 24-h pH values were much higher before cure (median, 5.15; 95% confidence interval (CI), 4.3-6.0) than 4 wk (3.6; 2.1-4.4) and 52 wk after cure (3.0; 2.1-4.4). The activity of corpus and antral **gastritis** was not assocd. with the magnitude of H+ change induced by omeprazole. The increased pH produced by omeprazole during H. pylori infection is likely to be due to neutralizing substances produced by H. pylori and not to H. pylori-induced **gastritis**.

L10 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:532139 HCAPLUS

DOCUMENT NUMBER: 125:185471

TITLE: Effects of misoprostol on healing and prevention of biopsy-induced **gastroduodenal** lesions occurring during the administration of diclofenac to volunteers

AUTHOR(S): Dorta, G.; Nicolet, M.; Vouillamoz, D.; Margalith, D.; Blum, A. L.; Armstrong, D.

CORPORATE SOURCE: Division de Gastroenterologie, CHUV, Lausanne, 1011, Switz.

SOURCE: Aliment. Pharmacol. Ther. (1996), 10(4), 563-569  
 CODEN: APTHEN; ISSN: 0269-2813

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To det. whether misoprostol promotes the healing of non-steroidal anti-inflammatory drug induced **gastroduodenal** lesions in a human exptl. model. Mucosal damage and healing of mucosal biopsy sites were assessed endoscopically in 10 healthy, **Helicobacter pylori**-neg. volunteers with a normal initial endoscopy: they were enrolled in a double-blind, double-dummy, placebo-controlled cross-over study. They received 2-wk courses of misoprostol (200 .mu.g b.d.) or placebo: a water-sol. non-steroidal antiinflammatory drug diclofenac 50 mg t.d.s., was given during the second week of each dosage regimen after three endoscopic biopsies had been taken from each of the duodenum, antrum and corpus. The no. of unhealed biopsy sites was not different after misoprostol or placebo, although the no. of healed biopsy sites was greater in the corpus and duodenum than in the antrum. Misoprostol did not prevent the appearance of diclofenac-induced erosions and petechiae. Epigastric discomfort was related to the intake of diclofenac and was reduced by misoprostol. Bloating and flatulence occurred more frequently with misoprostol alone and with misoprostol plus diclofenac, than with placebo alone or placebo plus diclofenac. Misoprostol does not prevent

new mucosal lesions induced by diclofenac in healthy volunteers and it does not accelerate the healing of the biopsy sites. Misoprostol decreases the frequency of diclofenac induced epigastric discomfort, but it increases gas bloating and flatulence.

L10 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:286501 HCAPLUS  
DOCUMENT NUMBER: 125:2539  
TITLE: Optimized BlaM-transposon shuttle mutagenesis of **Helicobacter pylori** allows the identification of novel genetic loci involved in bacterial virulence  
AUTHOR(S): Odenbreit, Stefan; Till, Markus; Haas, Rainer  
CORPORATE SOURCE: Max-Planck-Institut Biologie, Abteilung Infektionsbiologie, Tuebingen, D-72076, Germany  
SOURCE: Mol. Microbiol. (1996), 20(2), 361-373  
CODEN: MOMIEE; ISSN: 0950-382X  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB **Helicobacter pylori** is an important etiol. agent of **gastroduodenal** disease in humans. This report describes a general genetic approach for the identification of genes encoding exported proteins in *H. pylori*. The novel TnMax9 mini-blaM transposon was used for insertion mutagenesis of a *H. pylori* gene library established in *Escherichia coli*. A total of 192 *E. coli* clones expressing active .beta.-lactamase fusion proteins (BlaM+) were obtained, indicating that the corresponding target plasmids carry *H. pylori* genes encoding putative extracytoplasmic proteins. Natural transformation of *H. pylori* P1 or P12 using the 192 mutant plasmids resulted in 135 distinct *H. pylori* mutant strains (70%). Screening of the *H. pylori* collection of mutant strains allowed the identification of mutant strains impaired in motility, in natural transformation competence, and in adherence to **gastric** epithelial cell lines. Motility mutants could be grouped into distinct classes: (i) mutant strains lacking the major flagellin subunit FlaA and intact flagella (class I); (ii) mutant strains with apparently normal flagella, but reduced motility (class II), and (iii) mutant strains with obviously normal flagella, but completely abolished motility (class III). Two independent mutations that exhibited defects in natural competence for genetic transformation mapped to different genetic loci. In addn., 2 independent mutant strains were isolated by their failure to bind to the human **gastric** carcinoma cell line KatoIII. Both mutant strains carried a transposon in the same gene, 0.8 kb apart, and showed decreased autoagglutination when compared to the wild-type strain.

L10 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:194569 HCAPLUS  
DOCUMENT NUMBER: 124:278684  
TITLE: **Helicobacter pylori** augments the pH-increasing effect of omeprazole in patients with duodenal **ulcer**  
AUTHOR(S): Labenz, Joachim; Tillenburg, Birgit; Peitz, Ulrich; Idstroem, Jan-Peter; Verdu, Elena F.; Stolte, Manfred; Boersch, Gereon; Blum, Andre L.  
CORPORATE SOURCE: Department Internal Medicine and Gastroenterology, Elisabeth Hospital, Essen, Germany

SOURCE: Gastroenterology (1996), 110(3), 725-32  
CODEN: GASTAB; ISSN: 0016-5085

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Omeprazole is less effective in healthy subjects than in patients with duodenal **ulcers**. The aim of this study was to det. whether **Helicobacter pylori** augments the pH-increasing effect of omeprazole in patients with duodenal **ulcers**. In 16 patients with duodenal **ulcers**, baseline intragastric acidity was measured before and 4-6 wk after the cure of H. pylori infection. In 17 patients with duodenal **ulcers**, 24-h pH metry was performed during treatment with 20 mg omeprazole once daily before as well as after eradication of H. pylori. Intragastric acidity was measured using a glass electrode placed 5 cm below the cardia. H. pylori infection was assessed by [13C] urea breath test, culture, histol., and rapid urease test. H. pylori eradication resulted in a marked decrease of the pH-increasing effect of omeprazole (24-h median **gastric** pH, 5.5 vs. 3.0;  $P < 0.002$ ) that was most pronounced during nighttime (median **gastric** pH, 6.4 vs. 2.1;  $P = 0.001$ ). On the other hand, baseline intragastric pH remained unchanged after eradication (median **gastric** pH, 1.0 vs. 1.1;  $P = 0.5$ ). In patients with duodenal **ulcers** treated with omeprazole, intragastric pH depends significantly on the presence or absence of H. pylori, whereas baseline pH remained unchanged after H. pylori eradication.

L10 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:69418 HCAPLUS

DOCUMENT NUMBER: 124:193910

TITLE: Effect of curing **Helicobacter pylori** infection on intragastric pH during treatment with omeprazole

AUTHOR(S): Verdu, E F; Armstrong, D; Idstrom, J-P; Labenz, J; Stolte, M; Dorta, G; Borsch, G; Blum, A L

CORPORATE SOURCE: Division de Gastroenterologie, CHUV, Lausanne, 1011, Switz.

SOURCE: Gut (1995), 37(6), 743-8  
CODEN: GUTTAK; ISSN: 0017-5749

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB It has been shown that omeprazole treatment produces higher intragastric pH values in **Helicobacter pylori** pos. subjects than in H pylori neg. subjects. This study aimed to investigate the effect of curing H pylori on the intragastric pH in both the presence and absence of omeprazole therapy. Twenty four hour intragastric pH recordings were performed before and after a one week course of omeprazole (20 mg once daily) in 18 H pylori pos. subjects and were repeated after the infection had been cured. In the absence of omeprazole, the total 24 h pH values before cure did not differ from those afterwards. During omeprazole treatment the 24 h pH values were much higher before (median 95% CI), than after cure of infection ( $p < 0.001$ ). The omeprazole induced fall in H<sup>+</sup> activity before cure of H pylori did not, however, differ from that afterwards. It is concluded that the apparently greater antisecretory effect of omeprazole during H pylori infection may be a result of the prodn. of acid neutralizing compds. by the H pylori. Although a direct

interaction between H pylori and omeprazole cannot be excluded, it seems unlikely.

L10 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:852008 HCAPLUS  
DOCUMENT NUMBER: 123:237791  
TITLE: Urease-based vaccine and treatment for **Helicobacter** infection  
INVENTOR(S): **Michetti, Pierre**; Corthesy-Theulaz, Irene;  
Blum, Andre; Davin, Catherine; Haas, Rainer;  
Kraehenbuhl, Jean-Pierre; Saraga, Emilia  
PATENT ASSIGNEE(S): Oravax, Inc., USA  
SOURCE: PCT Int. Appl., 114 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522987	A1	19950831	WO 1995-US2202	19950223
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6290962	B1	20010918	US 1994-200346	19940223
AU 9519681	A1	19950911	AU 1995-19681	19950223
AU 694195	B2	19980716		
EP 751786	A1	19970108	EP 1995-912583	19950223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9506884	A	19970819	BR 1995-6884	19950223
JP 09509661	T2	19970930	JP 1995-522429	19950223
PL 179149	B1	20000731	PL 1995-316007	19950223
NO 9603508	A	19961021	NO 1996-3508	19960822
FI 9603281	A	19961022	FI 1996-3281	19960822
PRIORITY APPLN. INFO.:			US 1994-200346	A 19940223
			US 1992-970996	B2 19921103
			US 1993-85938	A2 19930706
			WO 1995-US2202	W 19950223
AB			A method of eliciting in a mammalian host a protective immune response to <b>Helicobacter</b> infection and treatment of <b>Helicobacter</b> infection by administering to the host an immunogenically effective amt. of a <b>Helicobacter</b> urease or urease subunits as antigen is described. Vaccine compns. are also provided.	

L10 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:451085 HCAPLUS  
DOCUMENT NUMBER: 121:51085  
TITLE: Genetic analysis of the **Helicobacter pylori** vacuolating cytotoxin: structural similarities with

AUTHOR(S): the IgA protease type of exported protein  
Schmitt, Wolfgang; Haas, Rainer  
CORPORATE SOURCE: Abt. Infektionsbiol., Max-Planck-Inst. Biol.,  
Tuebingen, D-72076, Germany  
SOURCE: Mol. Microbiol. (1994), 12(2), 307-19  
CODEN: MOMIEE; ISSN: 0950-382X  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The human **gastric** bacterial pathogen **Helicobacter pylori** has been implicated in type B **gastritis**, peptic **ulceration** and **gastric** adenocarcinoma. Here the authors report on the cloning and genetic characterization of an *H. pylori* gene named *vacA*, which encodes the vacuolating cytotoxin VacA, a novel type of antigenic bacterial toxin that induces the formation of intracellular vacuoles in epithelial cells. The vacuolating cytotoxin activity is expressed by a subset of clin. isolates (Vac+), all of which produce the 87 kDa cytotoxin antigen, but strains which produce neither the activity nor the cytotoxin protein (Vac-) also carry the gene. Isogenic *H. pylori* mutants in *vacA* generated by transposon shuttle mutagenesis produce neither the VacA antigen nor a vacuolating activity in a cell culture model. The *vacA* gene itself encodes a precursor protein of 139.6 kDa consisting of a 33-amino acid signal sequence, the 87 kDa cytotoxin and a 50 kDa C-terminal domain with features typical of a bacterial outer membrane protein. The VacA precursor shows no significant primary sequence homol. with any previously reported protein, but its structural organization closely resembles the IgA protease-type of exoprotein produced by pathogenic *Neisseriae* and *Haemophilus* species. The authors' current data support a model for secretion of the cytotoxin through the two bacterial membranes which involves the 30 kDa domain for outer membrane translocation with subsequent proteolytic cleavage and release of the mature 87 kDa cytotoxin into the extracellular environment.

L10 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1993:487670 HCAPLUS  
DOCUMENT NUMBER: 119:87670  
TITLE: Cloning and genetic characterization of a  
**Helicobacter pylori** flagellin gene  
AUTHOR(S): Leying, H.; Suerbaum, S.; Geis, G.; Haas, R.  
CORPORATE SOURCE: Abt. Infektionsbiol., Max-Planck-Inst. Biol.,  
Tuebingen, D-7400, Germany  
SOURCE: Mol. Microbiol. (1992), 6(19), 2863-74  
CODEN: MOMIEE; ISSN: 0950-382X  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB **Helicobacter pylori** produces polar sheathed flagella, which are believed to be essential for the bacterial colonization of the human **gastric** mucosa. Here the authors report on the cloning and genetic characterization of a *H. pylori* gene encoding the subunit of the flagellar filament, the flagellin. Screening of a genomic library of *H. pylori* with an oligonucleotide probe derived from the N-terminal amino acid sequence of purified flagellin resulted in a recombinant plasmid clone carrying the flagellin-encoding gene *flaA* on a 9.3 kb BglIII fragment. The nucleotide sequence of *flaA* revealed an open reading frame of 1530 nucleotides, encoding a protein with a predicted mol. mass of 53.2



kDa, which is similar in size with the purified flagellin protein in SDS-polyacrylamide gel electrophoresis. Sequence alignment of *H. pylori* flagellins demonstrates a high degree of similarity in the amino-terminal and carboxy-terminal regions, including those of the closely related genus *Campylobacter* (56% overall identity with *Campylobacter coli* flaA), but little homol. in the central domain. Southern hybridizations of chromosomal DNA with flaA-specific probes did not reveal the presence of addnl. homologous flagellin genes in *H. pylori*. Sequence anal. of the flaA flanking regions and mapping of the flaA mRNA start site by a primer extension expt. indicated that transcription of the gene is under the control of a  $\sigma_{28}$ -specific promoter sequence in *H. pylori*. The region upstream of the flaA promoter is subject to local DNA modification, resulting in the masking of two out of three closely linked HindIII restriction sites in the chromosome of strain 898-1. *Escherichia coli* strains harboring the recombinant plasmid did not produce full-length flagellin and data obtained with FlaA fusion proteins using an *E. coli* plasmid expression system suggest that a distinct nucleotide sequence in the gene interferes with productive translation of this protein in *E. coli*.

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L2 461 SEA FILE=REGISTRY UREASE/BI

L3 1 SEA FILE=REGISTRY "CAGA PROTEIN (HELICOBACTER PYLORI GENE CAGA)"/CN

L4 1 SEA FILE=REGISTRY "UREASE B (HELICOBACTER PYLORI STRAIN HPK5 GENE UREB)"/CN

L5 6043 SEA FILE=HCAPLUS L1 OR L2 OR L3 OR L4 OR (H OR HELICOBACTER?) (W) UREASE?

L6 1488 SEA FILE=HCAPLUS VACCIN? AND (?GASTR? OR ULCER? OR ?DYSPEPSIA? OR METAPLASIA OR ?LYMPHOMA?)

L7 63 SEA FILE=HCAPLUS L5 AND L6

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L7 ANSWER 1 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:504552 HCAPLUS

TITLE: HP30 and HP56 genes and proteins from Helicobacter pylori and their use to induce immune responses to Helicobacter cells or antigens

INVENTOR(S): Tian, Jing-Hui; Walker, Richard; Jackson, W. James

PATENT ASSIGNEE(S): Antex Biologics, Inc., USA

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Searched by Mona Smith

WO 2002051237 A2 20020704 WO 2001-US48392 20011207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

## PRIORITY APPLN. INFO.:

US 2000-732091 A 20001207

AB The invention discloses *Helicobacter pylori* HP30 or HP56 polypeptide, polypeptides derived thereof (HP30-derived or HP56-derived polypeptides), nucleic acids encoding said polypeptides, antibodies that specifically bind the HP30, HP56, HP30-derived or HP56-derived polypeptides, and T cells specific for HP30, HP56, HP30-derived or HP56-derived polypeptide. Also disclosed are prophylactic or therapeutic compns., including immunogenic compns., e.g. **vaccines**, comprising HP30, HP56, HP30-derived or HP56-derived polypeptides, nucleic acids encoding the same or antibodies thereto. The invention addnl. discloses methods of inducing in animals an immune response to *Helicobacter* cells or antigens. Recombinant HP30 and HP56 show to ability to act as therapeutic agents to decrease or eliminate *H. pylori* colonization in mice previously infected with *H. pylori*. Fifty percent or more of animals **vaccinated** orally with recombinant HP30 and HP56 are protected against subsequent *H. pylori* **gastric** colonization, and the remaining animals are colonized at lower levels than mice immunized with crude *H. pylori* cell lysate.

IT 9002-13-5, Urease

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**vaccine** immunogens; HP30 and HP56 genes and proteins from *Helicobacter pylori* and their use to induce immune responses to *Helicobacter* cells or antigens)

L7 ANSWER 2 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:391748 HCAPLUS

DOCUMENT NUMBER: 136:400601

TITLE: *Helicobacter pylori* gene hcpA and cysteine rich protein A and diagnostic and therapeutic uses thereof

INVENTOR(S): Deml, Ludwig; Schneider, Wulf; Lehn, Norbert

PATENT ASSIGNEE(S): Germany

SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040516	A2	20020523	WO 2001-DE4303	20011115
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

Minnifield 09/955,739

PRIORITY APPLN. INFO.:

DE 2000-10056486 A 20001115

AB The H. pylori gene hcpA and two proteins encoded by this gene are disclosed. The nucleic acids and proteins may be used for diagnosis of H. pylori infection and for prevention of infection, e.g., by **vaccination**. Thus, HcpA was shown to be immunogenic in humans and to be useful as a diagnostic marker of H. pylori infection. HcpA-producing H. pylori induced a strong interferon .gamma. release in murine spleen cell cultures; knockout hcpA mutants of H. pylori did not. The HcpA mRNA contained an internal translation start codon which overlapped the signal peptide cleavage site region. The majority of H. pylori strains studied expressed the hcpA gene, but secretion of HcpA into the culture was strain-dependent. Secretion of HcpA was not dependent on the sec path nor the Cag app. The anti-H. pylori antibody titer correlated with the HcpA secretion. HcpA was strongly secreted in **ulcer** patients. The HcpA protein contains a coiled-coil C-terminus which may influence its export from the cell.

IT 428657-62-9 428657-64-1 428657-66-3  
428657-68-5 428657-70-9

RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(amino acid sequence; Helicobacter pylori gene hcpA and cysteine rich protein and diagnostic and therapeutic uses thereof)

IT 428657-61-8 428657-63-0 428657-65-2  
428657-67-4 428657-69-6

RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; Helicobacter pylori gene hcpA and cysteine rich protein and diagnostic and therapeutic uses thereof)

L7 ANSWER 3 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:51293 HCAPLUS

DOCUMENT NUMBER: 136:107468

TITLE: Improvement of oral **vaccines**

INVENTOR(S): Bumann, Dirk; Meyer, Thomas F.

PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der  
Wissenschaften e.V., Germany

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004017	A2	20020117	WO 2001-EP7784	20010706
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				

PRIORITY APPLN. INFO.:

EP 2000-114683 A 20000707

AB The present invention relates to a method for prepg. and improving oral **vaccines** by modifying polypeptides which comprise at least one immunogenic epitope, particularly at least one immunogenic T cell epitope. Mice were **intragastrically** immunized with 5 mg ovalbumin in 100 .mu.L phosphate-buffered saline contg. 3% sodium bicarbonate with 10.000 U cholera toxoid.

IT 9002-13-5, Urease

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(A and B; improvement of oral **vaccines**)

Minnifield 09/955,739

L7 ANSWER 4 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:830481 HCAPLUS

DOCUMENT NUMBER: 136:100739

TITLE: Helicobacter pylori infection, immune response and **vaccination**

AUTHOR(S): Lembo, A.; Caradonna, L.; Magrone, T.; Mastronardi, M. L.; Caccavo, D.; Jirillo, E.; Amati, L.

CORPORATE SOURCE: Max Planck Institut fur Immunbiologie, Freiburg I. B., Germany

SOURCE: Current Drug Targets: Immune, Endocrine and Metabolic Disorders (2001), 1(3), 199-208  
CODEN: CDTIBT; ISSN: 1568-0088

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. It is well known that abnormal immune responses may play a pathogenic role in the H. pylori-related **gastropathy**. Indeed, as far as humoral immune response is concerned, it is still debated whether specific anti-H. pylori antibodies have a protective or noxious effect in infected hosts. Besides proinflammatory cytokines released from macrophages, such as tumor-necrosis factor-.alpha. and interleukin-1.beta., and IFN-.gamma. derived from T-helper 1 lymphocytes, also interleukin-10, a product of T-helper 2 lymphocytes with antiinflammatory properties, seems to be surprisingly involved in the pathogenesis of H. pylori-induced **gastritis**. In addn., lipopolysaccharide derived from the outer membrane of H. pylori acts as a chemoattractant for monocytes and induces release of free radicals, interleukin-1.beta., interleukin-6, interleukin-8 and tumor necrosis factor-.alpha.. On the other hand, H. pylori lipopolysaccharide could be responsible for the increased polyamine concns. in the **gastric** mucosa and polyamines, such as putrescine, spermidine and spermine, could be involved in the increased cell proliferation and consequent possible neoplastic transformation of the **gastric** mucosa. Incubation of peripheral blood mononuclear cells with H. pylori increases significantly the surface expression of CD95 receptor (Fas), thus suggesting that these bacteria are able to induce apoptosis. In animal models, different types of **vaccination** have been investigated, including stimulation of nasal and rectal lymphoid tissue, as well as adoptive transfer of T cell from donors immunized with H. pylori. However, results obtained are frequently disappointing. In humans, urease of H. pylori was safely used as oral **vaccine** in the absence or presence of adjuvants with encouraging results. Finally, DNA **vaccines** could offer in the future advantages for prophylactic H. pylori eradication, esp. where population is infected by this microorganism since childhood.

IT 9002-13-5, Urease

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(Helicobacter; Helicobacter pylori infection, immune response and **vaccination**)

REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:816711 HCAPLUS

DOCUMENT NUMBER: 135:356756

TITLE: Helicobacter antigens

INVENTOR(S): Meyer, Thomas F.; Jungblut, Peter; Bumann, Dirk; Aebischer, Anton; Haas, Gaby; Zimny-Arndt, Ursula; Lamer, Stephanie; Karaali, Galip; Sabarth, Nicolas; Wendland, Meike

PATENT ASSIGNEE(S): Max-Planck-Gesellschaft Zur Foerderung Der

Searched by MonaSmith

Minnifield 09/955,739

SOURCE: Wissenschaften E.V., Germany; et al.  
PCT Int. Appl., 150 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083531	A1	20011108	WO 2001-EP4728	20010426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2000-108968 A 20000427  
EP 2001-1101439 A 20010123

AB Using proteomics, the authors disclose the identification of proteins expressed by cultivated Helicobacter cells and which preferably react with human antisera. These Helicobacter antigens are provided which are suitable as targets for the diagnosis, prevention or treatment of Helicobacter infections.

IT 9002-13-5, Urease  
RL: ANT (Analyte); ANST (Analytical study)  
(proteomic anal. of Helicobacter pylori proteins and antigens)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:300853 HCAPLUS

DOCUMENT NUMBER: 134:325198

TITLE: Treatment and prevention of Helicobacter infection with C-terminal fragments of recombinant Helicobacter catalase

INVENTOR(S): Doidge, Christopher Vincent; Webb, Elizabeth Ann; Rothel, Linda Joy; Sutton, Philip; Hazell, Stuart Lloyd

PATENT ASSIGNEE(S): Csl Limited, Australia; The University of New South Wales

SOURCE: PCT Int. Appl., 84 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029198	A1	20010426	WO 2000-AU1249	20001013
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

Searched by Mona Smith

Minnifield 09/955,739

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
EP 1222255 A1 20020717 EP 2000-969109 20001013  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: AU 1999-3471 A 19991015  
WO 2000-AU1249 W 20001013

AB An isolated polypeptide and immunogenic fragments thereof are described together with their variants and derivs. as novel immunogenic agents for treating or preventing Helicobacter infection in a mammalian host. The polypeptide comprises a C-terminal portion of a Helicobacter catalase (strain RU1 and strain HP921023), which portion lacks significant amino acid sequence identity with human catalase, wherein the polypeptide is other than full-length Helicobacter catalase. The antigenic prepn. comprising the C-terminal fragment of catalase is used in a **vaccine** compn. for oral, intranasal or **intragastic** administration which includes a mucosal adjuvant and Helicobacter lipopolysaccharide or urease. Helicobacter catalase may be administered as the sole active immunogen in a **vaccine** compn. or expressed by alive vector. Thus, recombinant catalase shown to be an effective protective antigen for immunization against H. pylori infection.

IT 336208-60-7P 336208-61-8P

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; treatment and prevention of Helicobacter infection with C-terminal fragments of recombinant Helicobacter catalase)

IT 9002-13-5, Urease

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(co-treatment with catalase; treatment and prevention of Helicobacter infection with C-terminal fragments of recombinant Helicobacter catalase)

IT 336208-58-3 336208-59-4

RL: BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; treatment and prevention of Helicobacter infection with C-terminal fragments of recombinant Helicobacter catalase)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:77363 HCAPLUS

DOCUMENT NUMBER: 135:148063

TITLE: Cloning and characterization of a 22 kDa outer-membrane protein (Omp22) from Helicobacter pylori

AUTHOR(S): Kim, Jang-Seong; Chang, Ji-Hoon; Seo, Won-Young; Yu, Gum-Ju; Chung, Soo-Il; Yum, Jung-Sun

CORPORATE SOURCE: Mogam Biotechnology Research Institute, Yongin, 449-910, S. Korea

SOURCE: Molecules and Cells (2000), 10(6), 633-641  
CODEN: MOCEEK; ISSN: 1016-8478

PUBLISHER: Springer-Verlag Singapore Pte. Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Helicobacter pylori is a causative agent of **gastritis** and peptic **ulceration** in humans. As the first step towards development of a **vaccine** against H. pylori infection, we have attempted to identify

protective antigens. A potential target of **vaccine** development would be a *H. pylori* specific protein, which is surface-exposed and highly antigenic. We identified a 22 kDa outer-membrane protein (Omp22) from *H. pylori*, which was highly immunoreactive. By screening a *H. pylori* genomic DNA library with rabbit anti-*H. pylori* outer-membrane protein antibodies, the omp22 gene was cloned and 1.4 kb of the nucleotide sequence was detd. One open reading frame, encoding a 179-residue polypeptide, was identified and the amino acid sequence deduced showed homol. with peptidoglycan-assocd. lipoproteins. The sequence was conserved among other *H. pylori* strains. Omp22 protein is expressed as a precursor polypeptide of 179 residues and undergoes lipid modification and cleavage of an 18 amino acid signal peptide to yield a mature protein. Omp22 protein in *H. pylori* as well as recombinant Omp22 protein expressed in *E. coli* was localized into the outer membrane and exposed on the cell surface. Omp22 may have the potential as a target antigen for the development of a *H. pylori* **vaccine**.

IT 352364-15-9

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(amino acid sequence; cloning and characterization of a 22 kDa outer-membrane protein (Omp22) from *Helicobacter pylori*)

IT 194675-00-8, DNA (*Helicobacter pylori* strain KCTC0217BP gene omp22 plus flanks)

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(nucleotide sequence; cloning and characterization of a 22 kDa outer-membrane protein (Omp22) from *Helicobacter pylori*)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:70328 HCAPLUS

DOCUMENT NUMBER: 135:179310

TITLE: Evaluation of factors that can affect protective immune responses following oral immunization of recombinant *Helicobacter pylori* urease apoenzyme

AUTHOR(S): Kim, Jang Song; Chang, Ji Hoon; Park, Eun Jeong; Chung, Soo Il; Yum, Jung Sun

CORPORATE SOURCE: Mogam Biotechnology Research Institute, Kyonggi, 449-910, S. Korea

SOURCE: Journal of Microbiology and Biotechnology (2000), 10(6), 865-872

CODEN: JOMBES; ISSN: 1017-7825

PUBLISHER: Korean Society for Applied Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *Helicobacter pylori* is the major cause of **gastritis**, peptic **ulcer**, and a principal risk factor for **gastric** cancer. As the first step towards a **vaccine** against *H. pylori* infection, *H. pylori* urease was expressed and purified as a recombinant apoenzyme (rUrease) in *E. coli*. In order to develop an effective immunization protocol using rUrease, the host immune responses were evaluated after the oral immunization of mice with rUrease preps. plus cholera toxin relative to various conditions, such as the phys. nature of the antigen, the frequency of the booster immunization, the dose of the antigen, and the route of administration. The protective efficacy was assessed using a quant. culture following an *H. pylori* SS1 challenge. It was demonstrated that rUrease, due to its particulate nature, was more superior than the UreB subunit as a **vaccine** antigen. The oral immunization of rUrease elicited significant systemic and secretory antibody responses,



and activated predominantly Th2-type cellular responses. The bacterial colonization was significantly reduced (.apprx.100-fold) in those mice immunized with three or four weekly oral doses of rUrease plus cholera toxin, when compared to the non-immunized/challenged controls. The protection correlated well with the elicited secretory IgA level against rUrease, and these secretory antibody responses were highly dependent on the frequency of the booster immunization, yet unaffected by the dose of the antigen (25-200 .mu.g). These results demonstrate the remarkable potential of rUrease as a **vaccine** antigen, thereby strengthening the possibility of developing an *H. pylori* **vaccine** for humans.

IT 9002-13-5, Urease

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)

(protective immune responses following oral immunization of recombinant *Helicobacter pylori* urease apoenzyme)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:6727 HCAPLUS

DOCUMENT NUMBER: 135:194111

TITLE: Evaluation of immune prophylaxis of recombinant urease subunit of *Helicobacter pylori*

AUTHOR(S): Shi, Li; Wang, Jide; Chen, Ye; Zhang, Zhenshu; Zhang, Yali; Zhang, Wandai; Zhou, Dianyuan

CORPORATE SOURCE: The Digestive Disease Institute of PLA, Nanfang Hospital, The First Military Medical University, Canton, 510515, Peop. Rep. China

SOURCE: Zhonghua Yixue Zazhi (2000), 80(11), 811-815

CODEN: CHHTAT; ISSN: 0376-2491

PUBLISHER: Zhonghua Yixue Zazhishe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The immune prophylaxis of recombinant urease subunit A and B was evaluated. The BALB/C mice were divided into 7 groups: neg. control group, control group with cholera toxin subunit B (CTB), control group with rUreA, control group with rUreB, exptl. group with rUreA + CTB and exptl. group with rUreB + CTB, exptl. group with sonicate + CTB, which were **gastrically** inoculated with 150 mL PBS, 5 .mu.g CTB, 50 .mu.g rUreA, 50 .mu.g rUreB, 50 .mu.g rUreA + CTB and 400 .mu.g sonicate + 5 .mu.g CTB, resp. Two weeks later, the mice were **gastrically** infected with *H. pylori* (107-108 PCU per time). Four, 8 and 12 wk later, the mice were killed and the immune protection of PBS, CTB, rUreA, rUreB, rUreA + CTB, rUreB + CTB and sonicate + CTB were evaluated by assay of the presence of *H. pylori* in **gastric** tissue stained with Giemsa by microscopy. The mice in the side-effecting groups of rUreA + CTB and rUreB + CTB were not infected with *H. pylori*. 12 Wk later, the mice in the 2 groups were killed, and the side effects of rUreA + CTB and rUreB + CTB were evaluated by the infiltration of inflammation cells in **gastric** tissue stained with HE by microscopy. The mice **gastrically** inoculated with CTB, rUreA or rUreB had significantly less *H. pylori*. The immune protective effect of rUreA, rUreB or sonicate of *H. pylori* combined with CTB was stronger than that of rUreA, rUreB or sonicate of *H. pylori* alone. The immune protective effect of rUreA + CTB occurred later than that of rUreB + CTB or sonicate of *H. pylori* + CTB. The mice immunized with rUreA + CTB, rUreB + CTB or sonicate of *H. pylori* + CTB were not completely protected from *H. pylori* infection.

IT 9002-13-5, Urease

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

Minnifield 09/955,739

(Biological study); PROC (Process)  
(recombinant gene; evaluation of immune prophylaxis of recombinant  
urease subunit of Helicobacter pylori in mice)

L7 ANSWER 10 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:861846 HCAPLUS

DOCUMENT NUMBER: 134:27474

TITLE: Essential genes of Helicobacter pylori and their gene  
products and the development of **vaccines** and  
antibiotics for diagnosis and treatment of infections

INVENTOR(S): Apfel, Heiko; Fuchs, Thilo M.; Gibbs, Carol P.; Hueck,  
Christoph J.; Meyer, Thomas F.

PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Forderung der  
Wissenschaften e.V., Germany; Creatogen G.m.b.H.

SOURCE: PCT Int. Appl., 376 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073502	A2	20001207	WO 2000-EP5024	20000531
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
DE 19924965	A1	20001207	DE 1999-19924965	19990531
DE 19927740	A1	20001221	DE 1999-19927740	19990617
DE 19934029	A1	20010125	DE 1999-19934029	19990721

PRIORITY APPLN. INFO.: DE 1999-19924965 A 19990531  
DE 1999-19927740 A 19990617  
DE 1999-19934029 A 19990721

AB The invention relates to methods for prepg. therapeutic, preventative and/or diagnostic agents for treating microbial infections and to methods for identifying and characterizing essential genes from Helicobacter pylori. The invention also relates to the identified nucleic acids which code for the essential gene products and to the polypeptides which are coded therefrom.

IT 179005-51-7 184050-46-2 184656-26-6  
186468-77-9 193830-72-7 193831-90-2  
193831-91-3 193832-07-4 193832-39-2  
193832-65-4 193833-80-6 193833-95-3  
193834-24-1 193835-88-0 193836-29-2  
193836-35-0 193837-28-4 193837-75-1  
193837-82-0 193838-20-9 193838-77-6  
193838-88-9 193839-00-8 193839-95-1  
193840-59-4 193841-35-9 193841-46-2  
193841-82-6 193842-22-7 193842-23-8  
193843-92-4 193844-38-1 193844-42-7  
193844-74-5 193844-77-8 193844-90-5  
193844-95-0 193845-41-9 208732-74-5, Protein  
GHPO 253 (Helicobacter pylori) 311354-99-1 311355-01-8  
311355-04-1 311355-12-1 311355-14-3

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311355-18-7 311355-22-3 311355-26-7  
 311355-33-6 311355-35-8 311355-39-2  
 311355-43-8 311355-47-2 311355-58-5  
 311355-62-1 311355-65-4 311768-65-7  
 311768-72-6

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (amino acid sequence; essential genes of *Helicobacter pylori* and their  
 gene products and development of **vaccines** and antibiotics for  
 diagnosis and treatment of infections)

IT 184050-45-1 184656-25-5 311354-92-4  
 311354-96-8 311354-97-9 311354-98-0  
 311355-00-7 311355-02-9 311355-03-0  
 311355-05-2 311355-06-3 311355-07-4  
 311355-08-5 311355-09-6 311355-10-9  
 311355-11-0 311355-13-2 311355-15-4  
 311355-16-5 311355-17-6 311355-19-8 31135  
 5-20-1 311355-21-2 311355-23-4  
 311355-24-5 311355-25-6 311355-27-8  
 311355-28-9 311355-29-0 311355-30-3  
 311355-31-4 311355-32-5 311355-34-7  
 311355-36-9 311355-37-0 311355-38-1  
 311355-40-5 311355-41-6 311355-42-7  
 311355-44-9 311355-45-0 311355-46-1  
 311355-48-3 311355-49-4 311355-50-7  
 311355-51-8 311355-52-9 311355-53-0  
 311355-54-1 311355-55-2 311355-56-3  
 311355-57-4 311355-59-6 311355-60-9  
 311355-61-0 311355-63-2 311355-64-3

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nucleotide sequence; essential genes of *Helicobacter pylori* and their  
 gene products and development of **vaccines** and antibiotics for  
 diagnosis and treatment of infections)

L7 ANSWER 11 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:821256 HCAPLUS

DOCUMENT NUMBER: 134:339313

TITLE: Transgenic plants as a potential source of an oral  
**vaccine** against *Helicobacter pylori*

AUTHOR(S): Brodzik, R.; Gaganidze, D.; Henning, J.; Muszynska,  
 G.; Koprowski, H.; Sirko, A.

CORPORATE SOURCE: Institute of Biochemistry and Biophysics, Polish  
 Academy of Sciences, Warsaw, 02-106, Pol.

SOURCE: Progress in Biotechnology (2000), 17(Food  
 Biotechnology), 35-42

CODEN: PBITE3; ISSN: 0921-0423

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Plants are one of several novel hosts that can be used for an inexpensive  
 prodn. of recombinant biopharmaceuticals such as **vaccines**.  
 There is evidence that oral immunization with *Helicobacter pylori* urease,  
 or its large subunit encoded by the ureB gene in the presence of oral  
 adjuvants, is a feasible strategy for the development of a **vaccine**  
 against this **gastric** pathogen. In this study we report on  
 cloning and expression of the *H. pylori* ureB gene in a low alkaloid line  
 of tobacco (*Nicotiana tabacum* cv. LA Burley 21) and in the cells of carrot  
 callus (*Daucus carota* cv. Dolanka). The evaluation of the UreB level in  
 transgenic tobacco plants and transformed carrot callus was accomplished

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and revealed expression levels sufficient for an immunol. study in lab. animals.

IT 9002-13-5, Urease

RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)

(gene for H. pylori; Transgenic plants as a potential source of an oral **vaccine** against Helicobacter pylori)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:790541 HCAPLUS

DOCUMENT NUMBER: 133:349132

TITLE: Helicobacter pylori antigens for mucosal **vaccination**

INVENTOR(S): Pappo, Jacques

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066624	A1	20001109	WO 2000-SE808	20000428
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: SE 1999-1548 A 19990429

AB The authors disclose the prepn. of a **vaccine** which comprises HpaA and HOP38 polypeptides of H. pylori. Oral immunization with HpaA and HOP38 provided synergistic protection against **gastric** infection.

IT 185858-42-8 185858-47-3 305872-58-6

305872-63-3 305872-65-5 306277-75-8

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(amino acid sequence; polypeptides of HpaA adhesin and HOP38 protein in relation to **vaccination** against Helicobacter pylori infection)

IT 305872-57-5 305872-59-7 305872-60-0

305872-61-1 305872-62-2 305872-64-4

305872-66-6

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(nucleotide sequence; polypeptides of HpaA adhesin and HOP38 protein in relation to **vaccination** against Helicobacter pylori infection)

IT 169875-77-8

RL: PRP (Properties)

(unclaimed protein sequence; helicobacter pylori antigens for mucosal **vaccination**)

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IT 171657-97-9

RL: PRP (Properties)

(unclaimed sequence; helicobacter pylori antigens for mucosal  
**vaccination**)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:668688 HCAPLUS

DOCUMENT NUMBER: 135:14761

TITLE: Quantitative and bioluminescent assay to measure  
efficacy of conventional and DNA **vaccinations**  
against Helicobacter pylori

AUTHOR(S): Ozpolat, B.; Rao, X. M.; Osato, M. S.; Graham, D. Y.;  
Lachman, L. B.

CORPORATE SOURCE: Department of Bioimmunotherapy, University of Texas M.  
D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Combinatorial Chemistry and High Throughput Screening  
(2000), 3(4), 289-302

CODEN: CCHSFU; ISSN: 1386-2073

PUBLISHER: Bentham Science Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Vaccination** against Helicobacter pylori using DNA sequences  
encoding Urease A and B subunits was compared to immunization with urease  
antigen and MTP-PE in a liposome formulation. To det. the effectiveness  
of a **vaccine** against H. pylori in a mouse model it is essential  
to quantify the no. of H. pylori remaining in the stomachs following  
challenge with an inoculum of live bacteria. Culture assays and enzymic  
assays produce inconsistent results often unsuitable to conclude if  
**vaccine** candidates are protective. To overcome this problem, we  
developed two assays: (1) a competitive quant. PCR using a colorimetric  
readout and (2) a non-competitive direct quant. PCR using a highly  
sensitive bioluminescent readout. The competitive PCR requires  
coamplification of a segment of the urease C sequence and an internal  
control std. in a competitive manner using a single set of primers. PCR  
products were quantified colorimetrically by an ELISA and compared with  
known quantities of the internal control std. added to the PCR reaction.  
The highly sensitive, bioluminescent assay measures the amplified DNA  
directly using a flash-type luminescent tag and a specific probe. The  
Sydney strain of H. pylori was used for the mouse infection model.  
Quantification of H. pylori by either the bioluminescent assay or the  
competitive PCR was reliable, specific and sensitive compared to quant.  
growth assays which often gave false results. The bioluminescent assay  
was much more sensitive and less labor/time intensive than the competitive  
PCR. The bioluminescent assay was able to quantitate as few as 100  
bacteria, while the competitive assay could not detect less than 103  
bacteria per mouse stomach. Quantification of H. pylori by bioluminescent  
assay was superior to the competitive assay and may be used for research  
applications, such as the development of **vaccines**, pathogenesis  
of **gastric** disease and monitoring of antibiotic treatment.

IT 9002-13-5, Urease

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)

(antigen of; quant. and bioluminescent assay to measure efficacy of  
conventional and DNA **vaccinations** against Helicobacter  
pylori)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L7 ANSWER 14 OF 63 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:351549 HCAPLUS  
DOCUMENT NUMBER: 133:16302  
TITLE: Protective activity of Helicobacter pylori antigen  
INVENTOR(S): Dunkley, Margaret; Harris, Simon  
PATENT ASSIGNEE(S): Cortecs (UK) Limited, UK  
SOURCE: PCT Int. Appl., 48 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029432	A1	20000525	WO 1999-GB3759	19991111
W: CN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1131346	A1	20010912	EP 1999-954221	19991111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-25184 A 19981117  
WO 1999-GB3759 W 19991111

AB The authors disclose the purifn. and protective activity of HP0310 antigen derived from H. pylori. In one example, mice received HP0310 via intra-Peyer's patch immunization. Immunized mice were protected against subsequent challenge infection with a heterologous strain.

IT **193833-86-2**  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(amino acid sequence; **vaccination** against HP0310 protein of Helicobacter pylori in relation to protection against)

IT **271755-30-7**  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; **vaccination** against HP0310 protein of Helicobacter pylori in relation to protection against)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 63 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:282541 HCAPLUS  
DOCUMENT NUMBER: 133:41845  
TITLE: Immunization with recombinant Helicobacter pylori urease in specific-pathogen-free rhesus monkeys (Macaca mulatta)  
AUTHOR(S): Solnick, Jay V.; Canfield, Don R.; Hansen, Lori M.; Torabian, Sima Z.  
CORPORATE SOURCE: Departments of Internal Medicine (Division of Infectious Diseases) and Medical Microbiology and Immunology, Davis School of Medicine, University of California, Davis, CA, 95616, USA  
SOURCE: Infection and Immunity (2000), 68(5), 2560-2565  
CODEN: INFIBR; ISSN: 0019-9567  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Immunization with urease can protect mice from challenge with Helicobacter pylori, though results vary depending on the particular **vaccine**,

challenge strain, and method of evaluation. Unlike mice, rhesus monkeys are naturally colonized with *H. pylori* and so may provide a better est. of **vaccine** efficacy in humans. The purpose of this study was to examine the effectiveness of *H. pylori* urease as a **vaccine** in specific-pathogen (*H. pylori*)-free rhesus monkeys. Monkeys raised from birth and documented to be free of *H. pylori* were **vaccinated** with **orogastric** or i.m. urease. Two control monkeys were sham **vaccinated**. All monkeys were challenged with a rhesus monkey-derived strain of *H. pylori*, and the effects of **vaccination** were evaluated by use of quant. cultures of **gastric** tissue, histol., and measurement of serum IgG and salivary IgA. Despite a humoral immune response, all monkeys were infected after *H. pylori* challenge, and there were no differences in the d. of colonization. Immunization with urease therefore does not fully protect against challenge with *H. pylori*. An effective **vaccine** to prevent *H. pylori* infection will require different or more likely addnl. antigens, as well as improvements in the stimulation of the host immune response.

## IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(immunization with recombinant urease in rhesus monkeys does not prevent infection by *Helicobacter pylori*)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:213598 HCAPLUS

DOCUMENT NUMBER: 133:3462

TITLE: Pilot study of phoP/phoQ-deleted *Salmonella enterica* serovar typhimurium expressing *Helicobacter pylori* urease in adult volunteers

AUTHOR(S): Angelakopoulos, Haroula; Hohmann, Elizabeth L.

CORPORATE SOURCE: Infectious Disease Division, Department of Medicine, Massachusetts General Hospital, Boston, MA, 02114, USA

SOURCE: Infection and Immunity (2000), 68(4), 2135-2141

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Attenuated *Salmonella enterica* serovar Typhi has been studied as an oral **vaccine** vector. Despite success with attenuated *S. enterica* serovar Typhimurium vectors in animals, early clin. trials of *S. enterica* serovar Typhi expressing heterologous antigens have shown that few subjects have detectable immune responses to vectored antigens. A previous clin. study of phoP/phoQ-deleted *S. enterica* serovar Typhi expressing *Helicobacter pylori* urease from a multicopy plasmid showed that none of eight subjects had detectable immune responses to the vectored antigen. To further define the variables important for engendering immune responses to vectored antigens in humans, six volunteers were inoculated with 5.times.10<sup>7</sup> to 8.times.10<sup>7</sup> CFU of phoP/phoQ-deleted *S. enterica* serovar Typhimurium expressing the same antigen. Two of the six volunteers had fever; none had diarrhea, bacteremia, or other serious side effects. The volunteers were more durably colonized than in previous studies of phoP/phoQ-deleted *S. enterica* serovar Typhi. Five of the six volunteers seroconverted to *S. enterica* serovar Typhimurium antigens and had strong evidence of anti-*Salmonella* mucosal immune responses by enzyme-linked immunospot studies. Three of six (three of five who seroconverted to *Salmonella*) had immune responses in the most sensitive assay of urease-specific Ig prodn. by blood mononuclear cells in vitro. One of these had a fourfold or greater increase in end-point Ig titer in

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serum vs. urease. Attenuated *S. enterica* serovar Typhimurium appears to be more effective than *S. enterica* serovar Typhi for engendering immune responses to urease. Data suggest that this may be related to a greater stability of antigen-expressing plasmid in *S. enterica* serovar Typhimurium and/or prolonged intestinal colonization. Specific factors unique to non-typhoidal salmonellae may also be important for stimulation of the **gastrointestinal** immune system.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(humoral immune response to oral immunization with phoP/phoQ-deleted *Salmonella typhimurium* vector expressing *Helicobacter pylori* urease)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:197597 HCAPLUS

DOCUMENT NUMBER: 132:249998

TITLE: *Helicobacter pylori* membrane antigen and its encoding gene and use as **vaccine**

INVENTOR(S): Murakami, Kazuhisa; Kobayashi, Yoshinao; Wakatsuki, Yoshio

PATENT ASSIGNEE(S): Shionogi Seiyaku K. K., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	JP 2000083671	A2	20000328	JP 1998-257343	19980911
AB	The gene encoding a 20-kDa <i>Helicobacter pylori</i> membrane antigen is isolated and characterized. The antigen (or protein HPS) can be used for developing diagnostic agents or <b>vaccine</b> against the <i>H. pylori</i> -assocd. diseases such as <b>gastritis</b> and duodenum <b>ulcer</b> .				
IT	262347-78-4 262347-79-5				
	RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(amino acid sequence; <i>Helicobacter pylori</i> membrane antigen and encoding gene and use as <b>vaccine</b> )				
IT	207892-87-3 262347-77-3				
	RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)				
	(nucleotide sequence; <i>Helicobacter pylori</i> membrane antigen and encoding gene and use as <b>vaccine</b> )				

L7 ANSWER 18 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:183432 HCAPLUS

DOCUMENT NUMBER: 133:130387

TITLE: Quantitation of *Helicobacter pylori* in the stomach using quantitative polymerase chain reaction assays

AUTHOR(S): Ozpolat, Bulent; Actor, Jeffrey K.; Rao, Xiao-Mei; Lee, Sangjun; Osato, Michael; Graham, David Y.; Lachman, Lawrence B.

CORPORATE SOURCE: Department of Bioimmunotherapy, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA



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SOURCE: Helicobacter (2000), 5(1), 13-21  
CODEN: HELIFL; ISSN: 1083-4389  
PUBLISHER: Blackwell Science, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Background. The d. of Helicobacter pylori is thought to correlate with the degree of inflammation and thus indirectly with the outcome of the infection. Rapid quant. assays of H. pylori in **gastric** or duodenal mucosa are lacking. The aim was to develop quant. assays using the polymerase chain reaction to assess the quantity of H. pylori in the **gastric** mucosa. Methods. Competitive PCR was based on coamplification of a segment of the ureC sequence and an internal control using a single set of primers. PCR products were quantified colorimetrically by an ELISA and compared with known quantities of the internal control std. added to the PCR reaction. The highly sensitive, noncompetitive PCR assay does not use coamplification and measures the amplified DNA sequence using a flash-type luminescent tag and a specific probe. The mouse infected model using H. pylori strain SS-1 was used to develop the assays. Results. Quantification of H. pylori using either the competitive or noncompetitive PCR was reliable, highly sensitive and specific. Conclusions. The ability to rapidly quantitate H. pylori from **gastric** mucosa should be useful to investigate the role of H. pylori d. and infection outcome, as well as to monitor the effectiveness of antibiotic treatment or **vaccines** against H. pylori.

IT 9002-13-5, Urease

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(**vaccination**; quantitation of Helicobacter pylori in the stomach using quant. polymerase chain reaction assays)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:81792 HCAPLUS

DOCUMENT NUMBER: 132:221054

TITLE: Identification of immunodominant antigens from Helicobacter pylori and evaluation of their reactivities with sera from patients with different **gastroduodenal** pathologies

AUTHOR(S): Kimmel, Brigitte; Bosserhoff, Armin; Frank, Rainer; Gross, Roy; Goebel, Werner; Beier, Dagmar

CORPORATE SOURCE: Theodor-Boveri-Institut für Biowissenschaften, Lehrstuhl für Mikrobiologie, Universität Würzburg, Würzburg, D-97074, Germany

SOURCE: Infection and Immunity (2000), 68(2), 915-920  
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Colonization of the **gastric** mucosa by H. pylori is the major cause of **gastroduodenal** pathologies in humans. Studying the outcome of the humoral immune response directed against this **gastric** pathogen may contribute substantially to **vaccine** development and to the improvement of diagnostic techniques based on serol. By using 2-dimensional gel electrophoresis, 29 proteins from H. pylori G27 were identified which strongly react with sera derived from H. pylori-infected patients suffering from different **gastroduodenal** pathologies. These antigens were characterized by mass spectrometry and proved to correspond to products of open reading frames predicted by the H. pylori genome sequence. The comparison of the antigenic patterns

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recognized by these sera revealed no assocn. of specific H. pylori antigens with antibodies in patients with particular **gastroduodenal** pathologies.

IT 9002-13-5, Urease

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(B subunit; immunodominant antigens from Helicobacter pylori and reactivities with sera from patients with different **gastroduodenal** pathol.)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:68353 HCAPLUS

DOCUMENT NUMBER: 132:127722

TITLE: Urease-based **vaccine** against Helicobacter infection

INVENTOR(S): Park, Jong Beak

PATENT ASSIGNEE(S): Cheil Jedang Corporation, S. Korea

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000003730	A1	20000127	WO 1998-KR216	19980716
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

AU 9884643 A1 20000207 AU 1998-84643 19980716

PRIORITY APPLN. INFO.: WO 1998-KR216 A 19980716

AB The present invention relates to a **vaccine** for generating protective immunity against Helicobacter infection in mammals comprising a polyaminoacid prepn. including epitopes exhibited by a Lactobacillus-derived urease in combination with a pharmaceutically acceptable carrier or diluent. The polyaminoacid prepn. comprises a purified Lactobacillus fermentum urease, Lactobacillus reuteri urease or subunits thereof. In addn., the present invention relates to a process for assaying protective immune response in mammals infected with Helicobacter which comprises detg. the presence of antibody reactive with epitopes exhibited by a urease endogenous to said Lactobacillus organism within a sample collected by **gastric** route of said mammals.

IT 9002-13-5, Urease

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(peptides of; Lactobacillus urease-based **vaccine** against Helicobacter infection)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:717837 HCAPLUS

Searched by Mona Smith

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DOCUMENT NUMBER: 131:314241  
TITLE: Stabilized protein crystals, formulations containing them and methods of making them  
INVENTOR(S): Margolin, Alexey L.; Khalaf, Nazer K.; St. Clair, Nancy L.; Rakestraw, Scott L.; Shenoy, Bhami C.  
PATENT ASSIGNEE(S): Altus Biologics Inc., USA  
SOURCE: PCT Int. Appl., 201 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955310	A1	19991104	WO 1999-US9099	19990427
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2330476	AA	19991104	CA 1999-2330476	19990427
AU 9937646	A1	19991116	AU 1999-37646	19990427
EP 1073421	A1	20010207	EP 1999-920064	19990427
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2002512949	T2	20020508	JP 2000-545510	19990427
US 2002045582	A1	20020418	US 1999-374132	19990810
PRIORITY APPLN. INFO.:			US 1998-83148P	P 19980427
			US 1998-224475	A2 19981231
			US 1997-70274P	P 19971231
			WO 1999-US9099	W 19990427

AB Methods are provided for the stabilization, storage, and delivery of biol. active macromols., such as proteins, peptides and nucleic acids. Methods are provided for the crystn. of proteins and nucleic acids and for the prepn. of stabilized protein or nucleic acid crystals for use in dry or slurry formulations in pharmaceutical and veterinary formulations, diagnostics, cosmetics, food, and agricultural feeds. The crystals are stabilized by addn. of excipients such as carbohydrates or by encapsulating them in a polymeric carrier. Methods are presented for encapsulating proteins, glycoproteins, enzymes, antibodies, hormones, and peptide crystals or crystal formulations into compns. for biol. delivery to humans and animals. Thus, lipase from *Candida rugosa* was dissolved in distd. water, treated with celite, adjusted to pH 4.8 with AcOH, filtered, ultrafiltered to remove proteins of <30 kDa mol. wt., and crystn. was initiated by addn. of 2-methyl-2,4-pentanediol. Sucrose was added to the mother liquor to a concn. of 10%, and the crystals were sepd. by centrifugation, suspended in EtOH, and air dried at room temp. Alternatively, the lipase crystals were crosslinked and encapsulated in lactic acid/glycolic acid copolymer; the microspheres formed were 90 .mu.m in diam.

IT 9002-13-5, Urease  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(stabilized protein crystals, formulations contg. them and methods of

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making them)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:709918 HCAPLUS

DOCUMENT NUMBER: 132:34431

TITLE: Urease-based mucosal immunization against Helicobacter heilmannii infection induces corpus atrophy in mice  
AUTHOR(S): Dieterich, Christine; Bouzourene, Hanifa; Blum, Andre L.; Cortesey-Theulaz, Irene E.

CORPORATE SOURCE: Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, CH-1011, Switz.

SOURCE: Infection and Immunity (1999), 67(11), 6206-6209  
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mucosal immunization with Helicobacter heilmannii urease B or H. pylori urease, given nasally with cholera toxin, protects BALB/c mice against H. heilmannii infection and reduces a preexisting infection. However, immunization aggravates **gastric** corpus atrophy. The authors' results underline the necessity of defining immunization regimens that do not enhance mucosal damage.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(B; urease-based mucosal immunization against Helicobacter heilmannii infection induces corpus atrophy in mice)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:640728 HCAPLUS

DOCUMENT NUMBER: 131:285387

TITLE: A preventive and therapeutic **vaccine** for Helicobacter pylori-associated diseases

INVENTOR(S): Kim, Byung-o; Lee, Byoung-kwang; Yoon, Suk-won; Park, Seung-kook; Yu, Young-hyo; Pyo, Suhkneung; Choi, Deok-joon; Shin, Sung-seup; Jung, Hyung-jin

PATENT ASSIGNEE(S): Daewoong Pharmaceutical Co., Ltd., S. Korea

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949890	A1	19991007	WO 1998-KR72	19980331
W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9865247	A1	19991018	AU 1998-65247	19980331

PRIORITY APPLN. INFO.: WO 1998-KR72 19980331

AB The present invention relates to a preventive and therapeutic **vaccine** for *H. pylori*-assocd. diseases which comprises an active ingredient of a chimeric protein consisting of adhesin, an antigenic protein of *H. pylori* and A2 and B subunits of *Vibrio cholerae* toxin as an adjuvant. Since the adhesin/CTXA2B chimeric protein can induce specific antibodies neutralizing *H. pylori*, it can be used as an active ingredient of diagnostic kit for *H. pylori* infection and preventive or therapeutic **vaccine** for *H. pylori*-assocd. diseases as well.

IT 245742-60-3P

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (amino acid sequence; preventive and therapeutic **vaccine** for *Helicobacter pylori*-assocd. diseases)

IT 245742-59-0P

RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); PROC (Process) (nucleotide sequence; preventive and therapeutic **vaccine** for *Helicobacter pylori*-assocd. diseases)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:554588 HCAPLUS

DOCUMENT NUMBER: 131:307575

TITLE: Isolation of recombinant protective *Helicobacter pylori* antigens

AUTHOR(S): Hocking, D.; Webb, E.; Radcliff, F.; Rothel, L.; Taylor, S.; Pinczower, G.; Kapouleas, C.; Braley, H.; Lee, A.; Doidge, C.

CORPORATE SOURCE: Research and Development Division, CSL Limited, Parkville, 3052, Australia

SOURCE: Infection and Immunity (1999), 67(9), 4713-4719  
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A total of seven clones producing both new and previously described *Helicobacter pylori* proteins were isolated from a library of *H. pylori* genomic DNA. The screening approach by which these proteins were detected relied on the use of antisera raised in mice **vaccinated** with *Helicobacter felis* sonicate plus cholera toxin, a regimen which protects mice from *H. pylori* challenge. This strategy was designed to maximize the possibility of obtaining antigens which might be capable of conferring protection from *H. pylori* infection. Two of the clones were shown to encode the urease enzyme and the heat shock protein HspB, which have already been identified as protective antigens. The other five clones were sequenced, protein coding regions were deduced, and these sequences were amplified by PCR for incorporation into *Escherichia coli* expression vectors. The proteins produced from these expression systems were purified to allow testing for protective efficacy in an *H. pylori* mouse model. All five proteins were able to facilitate the clearance of a challenge with *H. pylori*, as judged by an assay of **gastric** urease activity and light microscopy on stomach sections. These results clearly indicate that the screening strategy has successfully identified candidate **vaccine** antigens.

IT 184050-44-0 184050-46-2 184050-48-4

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184050-50-8 247164-89-2 247215-98-1

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)

(amino acid sequence; isolation of recombinant protective Helicobacter  
pylori antigens)

IT 186291-43-0, GenBank U86607 186291-44-1, GenBank U86608

186291-45-2, GenBank U86609 186291-46-3, GenBank U86610

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)

(nucleotide sequence; isolation of recombinant protective Helicobacter  
pylori antigens)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 25 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:468005 HCAPLUS

DOCUMENT NUMBER: 131:127560

TITLE: Cloning and characterization of the Helicobacter  
pylori cagI region 5' to the cagA gene and its  
therapeutic uses

INVENTOR(S): Covacci, Antonello

PATENT ASSIGNEE(S): Chiron S.P.A., Italy

SOURCE: U.S., 252 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5928865	A	19990727	US 1995-477451	19950607
EP 967279	A1	19991229	EP 1999-202698	19930302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 2000333686	A2	20001205	JP 2000-126696	19930302
JP 2000350591	A2	20001219	JP 2000-126695	19930302
US 6090611	A	20000718	US 1995-471491	19950606
WO 9633274	A1	19961024	WO 1996-IB343	19960418
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
AU 9651605	A1	19961107	AU 1996-51605	19960418
EP 821735	A1	19980204	EP 1996-908300	19960418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506905	T2	19990622	JP 1996-531592	19960418
PRIORITY APPLN. INFO.:				
		IT 1992-FI52	A	19920302
		US 1995-425194	B2	19950420
		US 1995-471491	A2	19950606
		WO 1993-EP158	W	19930125
		EP 1993-905285	A3	19930302
		JP 1993-515309	A	19930302
		US 1995-477451	A	19950607
		WO 1996-IB343	W	19960418

AB Helicobacter pylori is known to cause or be a cofactor in type B  
gastritis, peptic ulcers, and gastric tumors.  
In both developed and developing countries, a high percentage of people

Searched by MonaSmith

are infected with this bacterium. The present invention relates generally to a certain *Helicobacter pylori* region located 5' to the CagA gene locus, to proteins encoded thereby, and to the use of these genes and proteins for diagnostic and **vaccine** applications. This region is present in type I *Helicobacter pylori* but absent from type II and appears to play a role in virulence.

IT 184491-44-9, Protein (*Helicobacter pylori* gene cagA-associated 3174-amino acid) 184539-26-2, Protein (*Helicobacter pylori* gene cagA-associated 3177-amino acid) 184539-31-9, Protein (*Helicobacter pylori* cagI region 1727-amino acid) 184539-32-0, Protein (*Helicobacter pylori* cagI region 1781-amino acid) 184539-33-1, Protein (*Helicobacter pylori* cagI region 1720-amino acid) 184539-34-2, Protein (*Helicobacter pylori* cagI region 1724-amino acid) 184539-35-3, Protein (*Helicobacter pylori* cagI region 1786-amino acid) 184594-41-0, Protein (*Helicobacter pylori* cagI region 1732-amino acid) 184594-43-2, Protein (*Helicobacter pylori* cagI region 464-amino acid) 184594-44-3, Protein (*Helicobacter pylori* cagI region 481-amino acid) 184594-45-4, Protein (*Helicobacter pylori* cagI region 471-amino acid) 184594-46-5, Protein (*Helicobacter pylori* cagI region 485-amino acid) 184594-47-6, Protein (*Helicobacter pylori* cagI region 469-amino acid) 184594-48-7, Protein (*Helicobacter pylori* cagI region 462-amino acid) 184594-50-1, Protein (*Helicobacter pylori* cagI region 396-amino acid) 184594-51-2, Protein (*Helicobacter pylori* cagI region 124-amino acid) 184594-52-3, Protein (*Helicobacter pylori* cagI region 382-amino acid) 184594-53-4, Protein (*Helicobacter pylori* cagI region 312-amino acid) 184594-54-5, Protein (*Helicobacter pylori* cagI region 131-amino acid) 184594-55-6, Protein (*Helicobacter pylori* cagI region 136-amino acid) 184594-56-7, Protein (*Helicobacter pylori* cagI region 79-amino acid) 184594-57-8, Protein (*Helicobacter pylori* cagI region 241-amino acid) 184594-58-9, Protein (*Helicobacter pylori* cagI region 131-amino acid) 184594-59-0, Protein (*Helicobacter pylori* cagI region 170-amino acid) 184594-61-4, Protein (*Helicobacter pylori* cagI region 143-amino acid) 184594-62-5, Protein (*Helicobacter pylori* cagI region 159-amino acid) 184594-63-6, Protein (*Helicobacter pylori* cagI region 140-amino acid) 184594-64-7, Protein (*Helicobacter pylori* cagI region 261-amino acid) 184594-68-1, Protein (*Helicobacter pylori* cagI region 122-amino acid) 184594-69-2, Protein (*Helicobacter pylori* cagI region 87-amino acid) 184594-70-5, Protein (*Helicobacter pylori* cagI region 178-amino acid)  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (amino acid sequence; cloning and characterization of *Helicobacter pylori* cagI region 5' to cagA gene and therapeutic uses)

IT 184594-42-1 234436-06-7 234436-07-8 234436-08-9  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)  
 (nucleotide sequence; cloning and characterization of *Helicobacter pylori* cagI region 5' to cagA gene and therapeutic uses)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 63 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:386468 HCAPLUS  
 DOCUMENT NUMBER: 131:255783  
 TITLE: *Helicobacter pylori* HspA heat-shock protein gene: cloning, expression and immunogenicity

Minnifield 09/955,739

AUTHOR(S): Li, Ming-Feng; Ling, Zhen; Zhang, Ying-Chun; Ma, Ai-Ying  
CORPORATE SOURCE: 455 Hospital of PLA, Shanghai, 200052, Peop. Rep. China  
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (1999), 31(3), 264-268  
CODEN: SHWPAU; ISSN: 0582-9879  
PUBLISHER: Shanghai Kexue Jishu Chubanshe  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

AB *Helicobacter pylori* is the causative agent of **gastritis** and peptic **ulcer** in human. The heat-shock protein A(HspA) may stimulate the immunoresponse protecting human body against challenge of *H. pylori*. The gene encoding the structural A subunit of *H. pylori* heat-shock protein was amplified from *H. pylori* chromosomal DNA by PCR, and was inserted in the prokaryotic expression vector pET-22b( + ), and then was transformed into the BL-21 (DE3)*E. coli* strain to express the HspA recombinant protein. HspA gene was measured to be 354 base pairs, and the recombinant protein gene encoded polypeptides of 118 amino acid residues, corresponding to calcd. mol. wt. of 15 kD. Western blot anal. of HspA recombinant protein was confirmed that it could be specifically recognized by the serum of *H. pylori*-infected patients, and could also be recognized by the serum of immunized Balb/c mice with HspA itself. This result suggests that HspA may be an effective protein **vaccine** for prevention and treatment of the infection of *H. pylori*.

IT 244756-02-3P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; *Helicobacter pylori* HspA heat-shock protein gene and cloning, expression and immunogenicity)

IT 244756-01-2

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
(nucleotide sequence; *Helicobacter pylori* HspA heat-shock protein gene and cloning, expression and immunogenicity)

L7 ANSWER 27 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:234184 HCAPLUS

DOCUMENT NUMBER: 131:72393

TITLE: Immunization with recombinant *Helicobacter pylori* urease decreases colonization levels following experimental infection of rhesus monkeys

AUTHOR(S): Lee, Cynthia K.; Soike, Kenneth; Hill, Joseph; Georgakopoulos, Kathleen; Tibbitts, Timothy; Ingrassia, Jennifer; Gray, Heather; Boden, James; Kleanthous, Harold; Giannasca, Paul; Ermak, Thomas; Weltzin, Richard; Blanchard, James; Monath, Thomas P.

CORPORATE SOURCE: OraVax, Inc., Cambridge, MA, USA

SOURCE: Vaccine (1999), 17(11-12), 1493-1505

CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rhesus monkeys, naturally colonized with *H. pylori* as indicated by culture and histol. were immunized with either 40 mg recombinant *H. pylori* urease administered orally together with 25 .mu.g *Escherichia coli* heat-labile enterotoxin (LT) or immunized with LT alone. An initial 6 doses were administered over an 8 wk period. All five **vaccinated** monkeys



had a greater than twofold rise in urease-specific serum IgG and IgA level and urease-specific salivary IgA was induced in 3 of 5 **vaccinated** animals after 6 or 7 doses of **vaccine**. **Vaccination** had no measurable therapeutic effect on *H. pylori* colonization. *H. pylori* was eradicated from these monkeys with a course of antimicrobials plus omeprazole, a 7th **vaccine** dose was given (10 mo after the 6th dose) and they were rechallenged with *H. pylori*. Necropsy was performed 23 wk after rechallenge and *H. pylori* colonization was detd. by histol. examn. of 12 individual **gastric** sites. A significant redn. in colonization (Friedman's anal. of variance) was found in the **vaccinated** animals. Histopathol. examn. of necropsy tissues also revealed a trend towards reduced **gastritis** and epithelial alterations in the **vaccinated** group compared to animals receiving LT alone. This study provides the first evidence for effective **vaccination** of nonhuman primates against *H. pylori*, and preliminary evidence that a redn. in bacterial d. attributable to immunization may lessen **gastric** inflammation.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(immunization with *Helicobacter pylori* urease decreases colonization levels following infection of rhesus monkeys)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 28 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:184151 HCAPLUS

DOCUMENT NUMBER: 130:227705

TITLE: Oral **vaccine** comprising *Lactobacillus* species transformed with **Helicobacter urease**

INVENTOR(S): Tabaqchali, Soad; Wilks, Mark

PATENT ASSIGNEE(S): Queen Mary & Westfield College, UK

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911284	A1	19990311	WO 1998-GB2631	19980902
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9888779	A1	19990322	AU 1998-88779	19980902
PRIORITY APPLN. INFO.:			GB 1997-18616	19970902
			WO 1998-GB2631	19980902

AB The present invention relates to a **vaccine** comprising a *Lactobacillus* species that contains a nucleotide sequence that encodes a urease peptide capable of initiating an anti-urease humoral and/or cellular immune response upon administration to a mammalian species. The **vaccine** may be used to treat **gastrointestinal** disorders, such as **gastritis**, that are the result of infection by

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Helicobacter strains, for which urease is the most prominent protein component.

IT 9002-13-5, Urease

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oral **vaccine** comprising Lactobacillus species transformed  
with **Helicobacter urease**)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 29 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:45201 HCAPLUS

DOCUMENT NUMBER: 130:123818

TITLE: Purified vacuolating toxin from Helicobacter pylori  
and methods to use antiserums to the antigen

INVENTOR(S): Cover, Timothy L.; Blaser, Martin J.

PATENT ASSIGNEE(S): Vanderbilt University, USA

SOURCE: U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 841,644.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5859219	A	19990112	US 1994-295643	19941027
WO 9316723	A1	19930902	WO 1993-US1558	19930224
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 6013463	A	20000111	US 1995-473265	19950607
PRIORITY APPLN. INFO.: US 1992-841644 19920226				
WO 1993-US1558 19930224				
US 1994-284747 19940802				

AB This invention relates to a purified Helicobacter pylori vacuolating toxin and methods to use this toxin to produce protective antibodies against H. pylori infection. Antiserum to this antigen can be used to detect the toxin. Methods to detect anti-toxin antibodies det. the susceptibility of a patient to develop peptic **ulcer** disease, **gastric** carcinoma, or other clin. consequences of H. pylori infection.

IT 219780-40-2P

RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU  
(Biological study, unclassified); PRP (Properties); BIOL (Biological  
study); OCCU (Occurrence); PREP (Preparation)  
(nucleotide sequence; purified vacuolating toxin from Helicobacter  
pylori and methods to use antiserums to the antigen)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 30 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:11297 HCAPLUS

DOCUMENT NUMBER: 130:181197

TITLE: Immunization of mice with urease **vaccine**  
affords protection against Helicobacter pylori  
infection in the absence of antibodies and is mediated  
by MHC class II-restricted responses

AUTHOR(S): Ermak, Thomas H.; Giannasca, Paul J.; Nichols,  
Richard; Myers, Gwendolyn A.; Nedrud, John; Weltzin,  
Richard; Lee, Cynthia K.; Kleanthous, Harold; Monath,

Minnifield 09/955,739

Thomas P.  
CORPORATE SOURCE: Ora Vax, Inc., Cambridge, MA, 02139, USA  
SOURCE: Journal of Experimental Medicine (1998), 188(12),  
2277-2288  
CODEN: JEMEAV; ISSN: 0022-1007  
PUBLISHER: Rockefeller University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB We examd. the roles of cell- and antibody-mediated immunity in urease **vaccine**-induced protection against *Helicobacter pylori* infection. Normal and knockout mice deficient in major histocompatibility complex (MHC) class I, MHC class II, or B cell responses were mucosally immunized with urease plus *Escherichia coli* heat-labile enterotoxin (LT), or parenterally immunized with urease plus aluminum hydroxide or a glycolipid adjuvant, challenged with *H. pylori* strain X47-2AL, and *H. pylori* organisms and leukocyte infiltration in the **gastric** mucosa quantified. In an adjuvant/route study in normal mice, there was a direct correlation between the level of protection and the d. of T cells recruited to the **gastric** mucosa. In knockout studies, oral immunization with urease plus LT protected MHC class I knockout mice [ $\beta$ 2-microglobulin (-/-)] but not MHC class II knockout mice [I-Ab (-/-)]. In B cell knockout mice [ $\mu$ .MT (-/-)], **vaccine**-induced protection was equiv. to that obsd. in immunized wild-type (+/+) mice; no IgA+ cells were detected in the stomach, but levels of CD4+ cells equiv. to those in the wild-type strain (+/+) were seen. These studies indicate that protection of mice against *H. pylori* infection by immunization with the urease antigen is dependent on MHC class II-restricted, cell-mediated mechanisms, and antibody responses to urease are not required for protection.

IT 9002-13-5, Urease

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(urease **vaccine** protects mice against *Helicobacter pylori* infection by MHC class II-restricted and antibody independent responses)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 31 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:684979 HCAPLUS

DOCUMENT NUMBER: 129:286736

TITLE: Recombinant *Helicobacter pylori* antigen-cholera toxin fusion proteins and their use as *H. pylori* **vaccines**

INVENTOR(S): Kim, Byung-o; Shin, Sung-seup; Yu, Young-hyo; Park, Myung-hwan; Choi, Dock-joon; Jung, Hyung-jin

PATENT ASSIGNEE(S): Daewoong Pharmaceutical Co., Ltd., S. Korea

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844130	A1	19981008	WO 1998-KR73	19980331
W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

Searched by Mona Smith

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

WO 9853082 A1 19981126 WO 1997-KR91 19970521

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9727937 A1 19981211 AU 1997-27937 19970521

AU 9865248 A1 19981022 AU 1998-65248 19980331

US 2001019834 A1 20010906 US 1999-402100 19990927

US 2002045218 A1 20020418 US 2001-760234 20010111

PRIORITY APPLN. INFO.:

KR 1997-11950 A 19970331

KR 1997-11951 A 19970331

WO 1997-KR91 A 19970521

WO 1998-KR73 W 19980331

US 1998-51315 B1 19980403

AB The present invention relates to chimeric proteins consisting of antigenic proteins of *Helicobacter pylori* and A2 and B subunits of *Vibrio cholerae* toxin, more specifically, to recombinant DNAs coding for antigenic proteins *Helicobacter pylori* and A2 and B subunits of *Vibrio cholerae* toxin, recombinant expression vectors contg. the genes, a process for prep. the chimeric proteins employing the recombinant microorganisms transformed with the said expression vectors, and preventive and therapeutic **vaccines** comprising the chimeric proteins for *Helicobacter pylori*-assocd. diseases. The recombinant DNAs which are designed for convenient expression and gene manipulation, can express chimeric proteins having excellent immunogenicity to *H. pylori*, which are stable in stomach, and penetrate mucous membrane of intestines easily, finally to stimulate prodn. of sIgA. Accordingly, the chimeric proteins expressed from the recombinant DNAs may be used as an active ingredient of a diagnostic kit for *H. pylori* infection and preventive or therapeutic **vaccine** for *H. pylori*-assocd. diseases, and may be used in the prodn. of anti-*H. pylori* antibody.

IT 214276-97-8P 214276-98-9P

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; recombinant *Helicobacter pylori* antigen-cholera toxin fusion proteins and their use as *H. pylori* **vaccines**)

IT 214276-92-3 214276-93-4

RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; recombinant *Helicobacter pylori* antigen-cholera toxin fusion proteins and their use as *H. pylori* **vaccines**)

L7 ANSWER 32 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:629229 HCAPLUS

DOCUMENT NUMBER: 130:79586

TITLE: Development of mouse and rat model of *Helicobacter pylori* infection

AUTHOR(S): Zeng, Zhirong; Hu, Pinjin; Chen, Minhu; Yu, Fengyan; Chen, Wei; Peng, Xiaozhong

CORPORATE SOURCE: Department of Gastroenterology, First Affiliated Hospital, Sun Yat-sen University of Medical Sciences, Canton, 510080, Peop. Rep. China

SOURCE: Zhonghua Yixue Zazhi (1998), 78(7), 494-497

CODEN: CHHTAT; ISSN: 0376-2491  
 PUBLISHER: Zhonghua Yixue Zazhi  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Chinese

AB Different rodent models of *H. pylori* infection were set up to meet different requirement for different purpose of study. Forty two-grade Wistar rats, 40 two-grade C57BL/6 mice and 40 SPF BALB/c mice were randomly divided into two groups: exptl. and control groups. Animals in the exptl. group were inoculated orally Hp strain (Sydney Strain 1, SS1), 0.4 mL of inoculum per mouse, 1.5 mL per rat (109 organisms/mL) 5 times for a week. Five animals in the exptl. and control groups were sacrificed resp. in 4, 8, 12 and 24 wk after the last bacteria inoculum. Histol. and Hp colonization were assessed by HE staining, Gimesa staining, Urease test, and Hp culture. Bacteria were clearly visible at antrum and body in all exptl. animals, but the no. of Hp colonization varied according to the animal strain in 4 wk. Heavy colonization was seen in C57BL/6 in antrum and body, and in BALB/c and Wistar colonization was located mainly at antrum, less at body, which tendered to increase over the expt. time, esp. in Wistar. Hp was neg. in the controls. All animals had no inflammatory changes in 4 wk, however, in 8, 12 and 24 wk in BALB/c, Wistar and C57BL/6 of the exptl. group, mild to moderate chronic active **gastritis** was obsd. in antrum and body, which increased to severity over time. Atrophy **gastritis** was still not seen in 24 wk. SS1 Hp can colonize in the glandular stomach mucosa of BALB/c, C57BL/6 mice and Wistar rats and lead to chronic active **gastritis** in long-term study. SS1 mouse and rat model is adaptable for animal expt. of *H. pylori* including **vaccine** studies, screening for novel therapeutics and investigation of mechanism of pathogenesis.

IT 9002-13-5, Urease  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
 BIOL (Biological study); OCCU (Occurrence)  
 (development of mouse and rat model of *Helicobacter pylori* infection)

L7 ANSWER 33 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:574857 HCAPLUS  
 DOCUMENT NUMBER: 129:288856  
 TITLE: Immunization against natural *Helicobacter pylori* infection in nonhuman primates  
 AUTHOR(S): Dubois, Andre; Lee, Cynthia K.; Fiala, Nancy;  
 Kleanthous, Harry; Mehlman, Patrick T.; Monath, Thomas  
 CORPORATE SOURCE: Laboratory of Gastrointestinal and Liver Studies,  
 Digestive Diseases Division, Department of Medicine,  
 Uniformed Services University of the Health Sciences,  
 , Bethesda, MD, 20814-4799, USA  
 SOURCE: Infection and Immunity (1998), 66(9), 4340-4346  
 CODEN: INFIBR; ISSN: 0019-9567  
 PUBLISHER: American Society for Microbiology  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB *Helicobacter pylori* infection is widespread in some breeding groups of a rhesus monkey colony (71% *H. pylori* pos. by 1 yr), and the rate of seroconversion is also high. As a result, these groups can be used to test the safety and efficacy of an anti-*H. pylori* **vaccine**. Nine-month-old female animals were randomized to receive either 8 mg of recombinant urease (rUre) plus 25 .mu.g of *Escherichia coli* heat-labile enterotoxin (LT) or placebo plus LT, given four times at 1-wk intervals followed by a booster 1 mo later. Ten months after the start of the immunization, the animals were subjected to endoscopy and biopsy samples were obtained. *H. pylori* negativity was defined as no *H. pylori* growth by culture and no *H. pylori* obsd. at histol. By this criterion, 2 (7%) of 29

animals receiving placebo and 8 (31%) of 26 immunized animals were H. pylori neg. In addn., antral **gastritis** score was significantly less in H. pylori-neg. immunized monkeys than in H. pylori-pos. animals, whether they were given rUre plus LT or placebo plus LT (or, resp.). Interestingly, antral **gastritis** was also significantly less in H. pylori-pos. animals given rUre plus LT than in H. pylori-pos. animals given placebo plus LT. However, quant. cultures did not demonstrate significant differences between the two latter groups. It is concluded that oral administration of rUre **vaccine** plus LT significantly protects nonhuman primates against H. pylori infection while not causing undesirable side effects.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(oral immunization with recombinant urease and enterotoxin protects rhesus monkeys against Helicobacter pylori infection)

L7 ANSWER 34 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:533739 HCAPLUS

DOCUMENT NUMBER: 130:2126

TITLE: Characterization of a Helicobacter pylori **vaccine** candidate by proteome techniques

AUTHOR(S): McAtee, C. Patrick; Young Lim, Moon; Fung, Kevin; Velligan, Mark; Fry, Kirk; Chow, Theresa P.; Berg, Douglas E.

CORPORATE SOURCE: Genelabs Technologies, 505 Penobscot Drive, Redwood City, CA, 94063, USA

SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1998), 714(2), 325-333  
CODEN: JCBBEP; ISSN: 0378-4347

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In a previous two-dimensional (2D) gel electrophoretic study of protein antigens of the **gastric** pathogen, Helicobacter pylori recognized by human sera, one of the highly and consistently reactive antigens, a protein with Mr of approx. 30,000 (Spot 15) seemed to be of special interest because of low yields on N-terminal protein sequencing. This suggested possible N-terminal modification, as the N-terminal sequence anal. of this 30,000 protein (Spot 15) did not provide a definitive match within the H. pylori genomic database. This protein was isolated by 2D polyacrylamide gel electrophoresis, evaluated by liq. chromatog.-mass spectrometry, and found to consist of two related species of approx. 28,100 and 26,500. In parallel, the proteins within this spot were digested in situ with the endoprotease Lys-C. Anal. of the Lys-C digest by matrix-assisted laser desorption time-of-flight mass spectrometry, peptide mapping, and sequence anal. was conducted. Comparison of the mass and sequence of the Lys-C peptides with those derived from a H. pylori genomic library identified an open reading frame of approx. 300 base pairs as the source of the Spot 15 protein. This corresponded to HP0175 in the recently reported H. pylori genome sequence, an open reading frame with some homol. to Campylobacter jejuni cell binding protein 2. Mass spectral and sequence anal. indicated that Spot 15 was a processed product generated by proteolytic cleavage at both the carboxy and amino termini of the 34 open reading frame precursor.

IT 215801-45-9

RL: PRP (Properties)

(amino acid sequence; characterization of Helicobacter pylori **vaccine** candidate by proteome techniques)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:377629 HCAPLUS  
 DOCUMENT NUMBER: 129:160371  
 TITLE: Systemic immunization with urease protects mice against Helicobacter pylori infection  
 AUTHOR(S): Guy, Bruno; Hessler, Catherine; Fourage, Sophie; Haensler, Jean; Vialon-Lafay, Elisabeth; Rokbi, Bachra; Millet, Marie-Jose Quentin  
 CORPORATE SOURCE: Research Department, Marcy l'Etoile, 69280, Fr.  
 SOURCE: Vaccine (1998), 16(8), 850-856  
 CODEN: VACCDE; ISSN: 0264-410X  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The ability of systemic immunization to induce protection against Helicobacter pylori infection has been evaluated in a mouse model. It was obsd. that if appropriate formulations and adjuvants were used such immunization elicited in outbred Swiss mice levels of protection similar or better than those induced by the oral route in the presence of cholera toxin or Escherichia coli heat labile toxin. Recombinant urease mixed with adjuvants, which induced strong Th1 and Th2 responses elicited better protection than urease mixed with adjuvants which induced a predominant Th2 type response only. These expts. demonstrate the feasibility of parenteral immunization against H. pylori and suggest that an appropriate balance between Th1 and Th2 type responses is required to achieve complete protection.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (systemic immunization with urease protects mice against Helicobacter pylori infection)

L7 ANSWER 36 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:363199 HCAPLUS  
 DOCUMENT NUMBER: 129:107724  
 TITLE: Rectal and intranasal immunizations with recombinant urease induce distinct local and serum immune responses in mice and protect against Helicobacter pylori infection  
 AUTHOR(S): Kleanthous, Harry; Myers, Gwendolyn A.; Georgakopoulos, Kathleen M.; Tibbitts, Timothy J.; Ingrassia, Jennifer W.; Gray, Heather L.; Ding, Ru; Zhang, Zhen-Zi; Lei, Wende; Nichols, Richard; Lee, Cynthia K.; Ermak, Thomas H.; Monath, Thomas P.  
 CORPORATE SOURCE: OraVax, Inc., Cambridge, MA, 02139, USA  
 SOURCE: Infection and Immunity (1998), 66(6), 2879-2886  
 CODEN: INFIBR; ISSN: 0019-9567  
 PUBLISHER: American Society for Microbiology  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB To det. the optimal inductive sites for immunization against H. pylori infection, the protective efficacy of recombinant urease (rUre) was assessed for mice given the vaccine by either the oral (p.o.), intranasal (i.n.), or rectal route. When mice were immunized with rUre (25 .mu.g p.o. or rectally or 10 .mu.g i.n.) plus heat-labile toxin from Escherichia coli as the mucosal adjuvant, all routes afforded protection against challenge with H. pylori, as indicated by a redn. in

**gastric** urease activity compared to that of sham-immunized controls. Quant. *H. pylori* culture of stomach tissue demonstrate a >97% redn. in bacterial burden in mice immunized by all routes. Induction of anti-urease IgA levels in **gastric** luminal secretions after p.o. immunization was greater than after i.n. administration (means, 6.0 and 1.02 ng/mL, resp.) and was dependent upon challenge with *H. pylori*. However, immunization by the rectal route resulted in the generation of the highest levels of **gastric** anti-urease IgA (mean, 40.89 ng/mL), which was detectable prior to challenge with *H. pylori*. Immunohistochem. staining of stomach tissue for cells secreting urease-specific antibody and CD4+ T cells showed levels of recruitment to be dependent upon challenge with *H. pylori* and equiv. for all routes. These results identify both the rectum and nasal passages as suitable inductive sites for urease immunization.

## IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(rectal and intranasal immunizations with recombinant urease induce local and serum immune responses in mice and protect against *Helicobacter pylori* infection)

L7 ANSWER 37 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:126362 HCAPLUS

DOCUMENT NUMBER: 128:191580

TITLE: Treatment and prevention of *Helicobacter* infection with recombinant *Helicobacter* catalase

INVENTOR(S): Doidge, Christopher Vincent; Lee, Adrian; Radcliff, Fiona Jane; Hazell, Stuart Lloyd

PATENT ASSIGNEE(S): CSL Limited, Australia; University of New South Wales

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9806853	A1	19980219	WO 1997-AU515	19970814
W: AU, CA, JP, KR, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6005090	A	19991221	US 1996-695987	19960815
AU 9737623	A1	19980306	AU 1997-37623	19970814
PRIORITY APPLN. INFO.:			US 1996-695987	19960815
			AU 1994-6124	19940608
			WO 1995-AU335	19950608
			WO 1997-AU515	19970814

AB An antigenic prepn. for use in the treatment or prevention of *Helicobacter* infection in a mammalian host, comprises recombinant catalase enzyme of *Helicobacter* bacteria, particularly recombinant catalase enzyme of *H. pylori* or *H. felis*, or an immunogenic fragment. Thus, an antigenic prepn. of catalase is used in a **vaccine** compn. for oral administration which includes a mucosal adjuvant such as cholera toxin. *Helicobacter* catalase may be administered as the sole active immunogen in a **vaccine** compn. or expressed by alive vector. Thus, catalase was purified from *H. pylori* (clin. strain 921023) and shown to immunize mice against infection by *H. pylori* or *H. felis*. *E. coli* clones expressing catalase from 2 different isolates of *H. pylori* (isolate RU1 and isolate 921023) were also characterized, and recombinant catalase shown to be an



Minnifield 09/955,739

- effective protective antigen for immunization against *H. pylori* infection.
- IT 203528-01-2 203528-02-3  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(amino acid sequence; treatment and prevention of *Helicobacter* infection with recombinant *Helicobacter* catalase)
- IT 9002-13-5, Urease  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(co-treatment with catalase; treatment and prevention of *Helicobacter* infection with recombinant *Helicobacter* catalase)
- IT 203527-99-5 203528-00-1  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; treatment and prevention of *Helicobacter* infection with recombinant *Helicobacter* catalase)

L7 ANSWER 38 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:63897 HCAPLUS

DOCUMENT NUMBER: 128:166039

TITLE: *Helicobacter pylori* adhesin binding fucosylated histo-blood group antigens revealed by retagging

AUTHOR(S): Ilver, Dag; Arnqvist, Anna; Ogren, Johan; Frick, Inga-Maria; Kersulyte, Dangeruta; Incecik, Engin T.; Berg, Douglas E.; Covacci, Antonello; Engstrand, Lars; Boren, Thomas

CORPORATE SOURCE: Dep. Microbiol., Umea Univ., Umea, SE-901 87, Swed.

SOURCE: Science (Washington, D. C.) (1998), 279(5349), 373-377  
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The bacterium *Helicobacter pylori* is the causative agent for peptic ulcer disease. Bacterial adherence to the human gastric epithelial lining is mediated by the fucosylated Lewis b (Leb) histo-blood group antigen. The Leb-binding adhesin, BabA, was purified by receptor activity-directed affinity tagging. The bacterial Leb-binding phenotype was assocd. with the presence of the *cag* pathogenicity island among clin. isolates of *H. pylori*. A vaccine strategy based on the BabA adhesin might serve as a means to target the virulent type I strains of *H. pylori*.

IT 203011-33-0 203011-34-1

RL: PRP (Properties)  
(amino acid sequence; *Helicobacter pylori* BabA adhesin binding fucosylated human blood group Leb antigen)

IT 200890-02-4

RL: PRP (Properties)  
(amino acid sequence; *Helicobacter pylori* BabA and BabB adhesins in binding fucosylated human blood group Leb antigen)

IT 200889-55-0, GenBank AF001388 202942-15-2

RL: PRP (Properties)  
(nucleotide sequence; *Helicobacter pylori* BabA adhesin binding fucosylated human blood group Leb antigen)

IT 202636-15-5, GenBank AF001389

RL: PRP (Properties)  
(nucleotide sequence; *Helicobacter pylori* BabA and BabB adhesins in binding fucosylated human blood group Leb antigen)

L7 ANSWER 39 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:15772 HCAPLUS

DOCUMENT NUMBER: 128:101086

Minnifield 09/955,739

TITLE: Helicobacter pylori blood group antigen-binding adhesin  
INVENTOR(S): Boren, Thomas; Arnqvist, Anna; Normark, Staffan; Ilver, Dag; Hammarstrom, Lennart  
PATENT ASSIGNEE(S): Boren, Thomas, Swed.; Arnqvist, Anna; Normark, Staffan; Ilver, Dag; Hammarstrom, Lennart  
SOURCE: PCT Int. Appl., 52 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9747646	A1	19971218	WO 1997-SE1009	19970610
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2257826	AA	19971218	CA 1997-2257826	19970610
AU 9731999	A1	19980107	AU 1997-31999	19970610
AU 726429	B2	20001109		
EP 909272	A1	19990421	EP 1997-927563	19970610
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2001503606	T2	20010321	JP 1998-501515	19970610
US 6410719	B1	20020625	US 1998-21560	19980210
PRIORITY APPLN. INFO.:			SE 1996-2287	A 19960610
			SE 1997-1014	A 19970319
			US 1997-41040P	P 19970321
			WO 1997-SE1009	W 19970610

AB A novel Helicobacter pylori blood group antigen binding (BAB) adhesin protein was isolated and purified, whereby said protein or fractions thereof bind specifically to fucosylated blood group antigens. The protein sequence of said adhesin is disclosed in this application. Simultaneously the DNA sequences for two genes, babA and babB, producing highly similar proteins, are disclosed. Said adhesin and/or DNA is useful for diagnose and therapy and/or prophylaxis directed against H. pylori induced infections, e.g. **gastritis** and acid peptic disease, i.e. active **vaccination**. A new Ig compn., which exhibits specific activity to a Lewisb antigen binding Helicobacter pylori adhesin, or preferably, monoclonal and/or polyclonal antibodies to said adhesin offer a new and more efficient method of treatment and/or prevention of **gastrointestinal** diseases, caused by Helicobacter pylori or other Helicobacter species, i.e. passive **vaccination**.

IT 200890-01-3 200890-02-4

RL: PRP (Properties)

(amino acid sequence; Helicobacter pylori blood group antigen-binding adhesin and antibody as active and passive **vaccines** in relation to)

IT 200889-55-0 200889-56-1

RL: PRP (Properties)

(nucleotide sequence; Helicobacter pylori blood group antigen-binding adhesin and antibody as active and passive **vaccines** in relation to)

L7 ANSWER 40 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:772606 HCAPLUS

DOCUMENT NUMBER: 128:58307

TITLE: Induced by Contact with Epithelium gene iceA of Helicobacter pylori, diagnosis of H. pylori infection, and treatment and prevention of peptic **ulcers**

INVENTOR(S): Miller, Geraldine G.; Peek, Richard M., Jr.; Thompson, Stuart A.; Blaser, Martin J.

PATENT ASSIGNEE(S): Vanderbilt University, USA; Miller, Geraldine G.; Peek, Richard M., Jr.; Thompson, Stuart A.; Blaser, Martin J.

SOURCE: PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9743901	A1	19971127	WO 1997-US8558	19970520
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5780278	A	19980714	US 1996-650528	19960520
CA 2227171	AA	19971127	CA 1997-2227171	19970520
AU 9730733	A1	19971209	AU 1997-30733	19970520
AU 736089	B2	20010726		
EP 861027	A1	19980902	EP 1997-925659	19970520
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 11511032	T2	19990928	JP 1997-542660	19970520
US 6004354	A	19991221	US 1998-60584	19980415
US 6107464	A	20000822	US 1999-413140	19991006

PRIORITY APPLN. INFO.:

US 1996-650528 A2 19960520

WO 1997-US8558 W 19970520

US 1998-60584 A3 19980415

AB A purified IceA protein of Helicobacter pylori is provided. The protein is expressed as either an IceA 1 or an IceA 2 variant. A purified polypeptide fragment of the IceA protein is also provided. An antigenic fragment of IceA is provided. An isolated nucleic acid that encodes an IceA protein of H. pylori is provided. A nucleic acid that encodes an IceA 1 variant and a nucleic acid that encodes an IceA 2 variant is also provided. Fragments of the IceA gene are provided. A method of detecting the presence of an antibody against H. pylori in a sample is provided. The method comprises the following steps: a) contacting the sample with a purified IceA protein of H. pylori or a H. pylori-specific fragment thereof; and b) detecting the binding of the antibody in the sample to the protein or fragment, the detection of binding indicating the presence in the sample of antibodies against H. pylori. A method of detecting the presence of an antibody against an **ulcerative** H. pylori strain in a sample is also provided. The reported expts. demonstrate that adherence of H. pylori to **gastric** epithelial cells induces strain-specific expression of a novel **ulcer**-assocd. gene, iceA, which exists in two major allelic variants. The increased expression of iceA following adherence and its assocn. with peptic **ulcer** disease suggest it may play a role in detg. increased virulence.

IT 200296-20-4 200296-21-5 200298-65-3

200358-91-4

RL: PRP (Properties)

(amino acid sequence; induced by Contact with Epithelium gene iceA of Helicobacter pylori, diagnosis of H. pylori infection, and treatment and prevention of peptic ulcers)

IT 200298-64-2 200298-66-4 200298-67-5  
200298-68-6 200298-69-7 200298-70-0  
200298-71-1 200298-72-2 200298-73-3, DNA  
(Helicobacter pylori gene iceA) 200298-74-4  
RL: PRP (Properties)

(nucleotide sequence; induced by Contact with Epithelium gene iceA of Helicobacter pylori, diagnosis of H. pylori infection, and treatment and prevention of peptic ulcers)

L7 ANSWER 41 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:677623 HCAPLUS

DOCUMENT NUMBER: 127:330049

TITLE: Gastritis in urease-immunized mice after Helicobacter felis challenge may be due to residual bacteria

AUTHOR(S): Ermak, Thomas H.; Ding, Ru; Ekstein, Bruce; Hill, Joseph; Myers, Gwendolyn A.; Lee, Cynthia K.; Pappo, Jacques; Kleanthous, Harold K.; Monath, Thomas P.

CORPORATE SOURCE: OraVax, Inc., Cambridge, MA, USA

SOURCE: Gastroenterology (1997), 113(4), 1118-1128

CODEN: GASTAB; ISSN: 0016-5085

PUBLISHER: Saunders

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Oral Immunization with recombinant Helicobacter pylori urease (rUre) coadministered with a mucosal adjuvant protects mice against challenge with Helicobacter felis. In this study, the duration of protection and gastritis after challenge were characterized at sequential time intervals up to 1 yr. Outbred Swiss-Webster mice were orally immunized with rUre plus adjuvant and examd. for the presence of H. felis infection and leukocyte infiltration into the gastric mucosa. When defined by gastric urease activity, 70%-95% of rUre-immunized mice were protected for between 2 and 57 wk. Challenge with H. felis increased the inflammatory response in the gastric mucosa of rUre-immunized mice, which also had elevated CD4+ and CD8+ T cells. The CD8+ cells represented a population of gastric intraepithelial cells, which expressed the mucosal .alpha.E-integrin. Epithelial changes consisting of parietal cell loss and hyperplasia of the epithelium occurred in approx. 20% of the mice. Antimicrobial triple therapy significantly decreased the degree of gastritis and epithelial alteration in the stomach. These results indicate that oral immunization of mice with rUre produces a long-lasting inhibition of H. felis infection but that residual bacteria may produce a persistent lymphocytic infiltration under these exptl. conditions.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(of Helicobacter pylori; gastritis in urease-immunized mice after Helicobacter felis challenge may be due to residual bacteria)

L7 ANSWER 42 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:655716 HCAPLUS

DOCUMENT NUMBER: 127:327220

TITLE: Characterization of Helicobacter pylori dapE and construction of a conditionally lethal dapE mutant

AUTHOR(S): Karita, Mikio; Etterbeek, Michele L.; Forsyth, Mark

Minnifield 09/955,739

CORPORATE SOURCE: H.; Tummuru, Murali K. R.; Blaser, Martin J.  
Division of Infectious diseases, Department of  
Medicine, Vanderbilt University School of Medicine,  
Nashville, TN, 37232-2605, USA  
SOURCE: Infection and Immunity (1997), 65(10), 4158-4164  
CODEN: INFIBR; ISSN: 0019-9567  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Helicobacter pylori colonizes the human **gastric** mucosa and causes **gastritis, ulceration, or gastric** cancer. A previously uncharacterized region of the H. pylori genome was identified and sequenced. This region includes a putative operon contg. three open reading frames termed gidA (1,866 bp), dapE (1,167 bp), and orf2 (753 bp); the gidA and dapE products are highly homologous to other bacterial proteins. In E. coli, dapE encodes N-succinyl-L-diaminopimelic acid desuccinylase, which catalyzes the hydrolysis of N-succinyl-L-diaminopimelic acid to L-diaminopimelic acid (L-DAP) and succinate. When wild-type H. pylori strains were transformed to selected for dapE mutagenesis, mutants were present when plates were supplemented with DAP but not with lysine; orf2 mutants were selected without DAP supplementation. Consistent with the finding that GidA is essential in Escherichia coli, the authors were unable to obtain a gidA mutant in H. pylori despite evidence that insertional mutagenesis had occurred. The position of gidA, dapE, and orf2 suggest that they form an operon, which was supported by slot blot RNA hybridization and reverse transcriptase PCR studies. The data imply that the H. pylori dapE mutant may be useful as a conditionally lethal **vaccine**.

IT 197983-20-3 197983-21-4 197983-22-5

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)

(amino acid sequence; characterization of Helicobacter pylori dapE and construction of conditionally lethal dapE mutant)

IT 194517-34-5, GenBank AF008565

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)

(characterization of Helicobacter pylori dapE and construction of conditionally lethal dapE mutant)

L7 ANSWER 43 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:506615 HCAPLUS

DOCUMENT NUMBER: 127:146507

TITLE: Helicobacter pylori oxidoreductase enzymes and their uses

INVENTOR(S): Chalk, Peter Andrew; Clayton, Christopher Leeson;  
Kelly, David Jacob; Hughes, Nicola Jane

PATENT ASSIGNEE(S): Glaxo Group Limited, UK; Chalk, Peter Andrew; Clayton,  
Christopher Leeson; Kelly, David Jacob; Hughes, Nicola  
Jane

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723626	A1	19970703	WO 1996-GB3119	19961217

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

Searched by Mona Smith

Minnifield 09/955,739

DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,  
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,  
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,  
MR, NE, SN, TD, TG

AU 9711854 A1 19970717 AU 1997-11854 19961217  
PRIORITY APPLN. INFO.: GB 1995-26407 19951222  
WO 1996-GB3119 19961217

AB Oxidoreductase enzymes have been identified in *H. pylori* and can be used to screen for agents effective against *H. pylori*-mediated diseases or disorders such as **gastritis** and **ulcers**. The preferred oxidoreductase enzymes are 2-oxoglutarate:ferredoxin oxidoreductase and pyruvate:flavodoxin oxidoreductase. These enzymes (and their constituent subunits) or derivs. or homologs of them can be used in pharmaceutical compns. or used as antibody Fab and Fv fragments to develop **vaccines** to *H. pylori*. The anti-*H. pylori* antibodies can be either monoclonal or polyclonal. Sequences of the genes and the corresponding proteins for both 4-subunit oxidoreductase enzymes were detd. Oxidoreductase inhibitors specific for the two claimed *H. pylori* enzymes can also be used as therapeutic agents.

IT **193226-92-5P**  
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(2-oxoglutarate (*Helicobacter pylori* OorC subunit) amino acid sequence; isolation, structure, and activity of *Helicobacter pylori* oxidoreductase enzymes and their use in screening for anti-*H. pylori* agents)

IT **193226-89-0P 193226-90-3P 193226-91-4P**  
**193226-94-7P 193226-95-8P 193226-96-9P**  
**193226-97-0P**  
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; isolation, structure, and activity of *Helicobacter pylori* oxidoreductase enzymes and their use in screening for anti-*H. pylori* agents)

IT **193226-88-9P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(nucleotide sequence; isolation, structure, and activity of *Helicobacter pylori* oxidoreductase enzymes and their use in screening for anti-*H. pylori* agents)

IT **193226-93-6P**  
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(nucleotide sequence; isolation, structure, and activity of *Helicobacter pylori* oxidoreductase enzymes and their use in screening for anti-*H. pylori* agents)

L7 ANSWER 44 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:347305 HCAPLUS

DOCUMENT NUMBER: 127:16332

TITLE: Studies on the outer membrane proteins of *Helicobacter pylori* as the **vaccine** antigens for oral administration

AUTHOR(S): Park, Hyung-Bae; Choe, Tae-Boo

CORPORATE SOURCE: Department of Microbiological Engineering, Konkuk University, Seoul, 143-701, S. Korea

Minnifield 09/955,739

SOURCE: Sanop Misaengmul Hakhoechi (1997), 25(2), 129-136  
CODEN: SMHAEH; ISSN: 0257-2389  
PUBLISHER: Korean Society for Applied Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: Korean

AB H. pylori is a spiral-shaped, microaerophilic human **gastric** pathogen causing chronic-active **gastritis** in assocn. with duodenal **ulcer** and **gastric** cancer. To investigate the possibility of H. pylori outer membrane proteins (OMPs) as the oral **vaccine** antigens, sarcosine-insol. outer membrane fraction was prepd. from H. pylori NCTC 11637. The major OMPs having apparent mol. masses of 62 kDa, 54 kDa, and 33 kDa were detected by SDS-PAGE, and were identified as urease B subunit (UreB), heat shock protein (Hsp54 kDa), and urease A subunit (UreA), resp. Minor protein bands of 57 kDa, 52 kDa, 40 kDa, 36 kDa, and 31 kDa were also obsd. The antigenicity of H. pylori OMPs and antigenic cross-reactivity among the strains were detd. by immunoblot anal. using anti-H. pylori OMPs antisera or intestinal lavage solns. The results showed that UreB, Hsp54 kDa, UreA, and 40 kDa proteins vigorously stimulated mucosal immune response rather than systemic immunity. These proteins thus seem to be useful as candidates for the oral **vaccine**. The immunoblotting results with surface proteins from 8 isolated H. pylori strains were similar to that of H. pylori NCTC 11637. The IgA which arose from oral administration of H. pylori OMPs, was able to bind H. pylori whole-cells.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(A and B subunits; outer membrane proteins of Helicobacter pylori as **vaccine** antigens for oral administration)

L7 ANSWER 45 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:229088 HCAPLUS

DOCUMENT NUMBER: 126:303498

TITLE: Localization of Helicobacter pylori urease and heat shock protein in human **gastric** biopsies

AUTHOR(S): Dunn, Bruce E.; Vakil, Nimish B.; Schneider, Barbara G.; Miller, Margaret M.; Zitzer, Jason B.; Peutz, Thomas; Phadnis, Suhas H.

CORPORATE SOURCE: Department of Pathology, Medical College of Wisconsin, Milwaukee, WI, 53295-1000, USA

SOURCE: Infection and Immunity (1997), 65(4), 1181-1188

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Helicobacter pylori is a spiral, gram-neg. bacterium which causes chronic **gastritis** and plays a crit. role in peptic **ulcer** disease, **gastric** carcinoma, and **gastric** **lymphoma**. H. pylori expresses significant urease activity which is an essential virulence factor. Since a significant fraction of urease activity is located on the surface of the bacterium, the urease mol. is a logical choice as an antigen for a **vaccine**; currently recombinant urease apoenzyme is being tested as a **vaccine** in phase II clin. trials. The authors have recently demonstrated that urease and HspB (a homolog of the GroEL heat shock protein) become assocd. with the surface of H. pylori in vitro in a novel manner: these cytoplasmic proteins are released by bacterial autolysis and become adsorbed to the surface of intact bacteria, reflecting the unique characteristics of the outer membrane. To det. if similar mechanisms are operative in vivo, the

authors detd. the ultrastructural locations of urease and HspB within bacteria present in human **gastric** biopsies. The results demonstrate that both urease and HspB are located within the cytoplasm of all bacteria examd. in human **gastric** biopsies. Interestingly, a significant proportion of the bacteria examd. also possessed variable amts. of surface-assocd. urease and HspB antigen (from 5-50% of the total antigenic material), indicating that in vivo, *H. pylori* has surface characteristics which enable it to adsorb cytoplasmic proteins. This is consistent with an altruistic autolysis model in which *H. pylori* uses genetically programmed bacterial autolysis to release urease and other cytoplasmic proteins which are subsequently adsorbed onto the surface of neighboring viable bacteria. These observations have important implications regarding pathogenesis and development of **vaccines** for *H. pylori*.

IT 9002-13-5, Urease

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(*Helicobacter pylori* urease and HspB protein localization in human stomach)

L7 ANSWER 46 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:124447 HCAPLUS

DOCUMENT NUMBER: 126:130583

TITLE: Compositions containing antigen and lipoprotein and adjuvant for inducing immunological response in host  
INVENTOR(S): Becker, Robert S.; Huebner, Robert C.; Gray, Maryann B.; Biscardi, Karen S.; Erdile, Lorne F.; Guy, Bruno

PATENT ASSIGNEE(S): Connaught Laboratories, Inc., USA

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640290	A1	19961219	WO 1996-US8866	19960605
W: AU, CA, FI, JP, NO				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6251405	B1	20010626	US 1995-476656	19950607
US 6379675	B1	20020430	US 1996-588621	19960119
AU 9661519	A1	19961230	AU 1996-61519	19960605
AU 717890	B2	20000406		
EP 831937	A1	19980401	EP 1996-919085	19960605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11510370	T2	19990914	JP 1996-501336	19960605
NO 9705620	A	19980204	NO 1997-5620	19971204
FI 9704423	A	19980204	FI 1997-4423	19971205

PRIORITY APPLN. INFO.:

US 1995-476656	A	19950607
US 1996-588621	A	19960119
WO 1996-US8866	W	19960605

AB **Vaccine** compns. contg. at least one antigen and at least one lipoprotein and optionally an adjuvant is disclosed. The lipoprotein can itself be antigenic or immunogenic. The antigen can be influenza hemagglutinin (HA) and the lipoprotein a recombinantly expressed product having an OspA leader for lipidation and PspA for the protein portion. The antigen can also be OspC and the lipoprotein OspA.

IT 9002-13-5, Urease



Minnifield 09/955,739

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(antigen; compns. contg. antigen and lipoprotein and adjuvant for  
inducing immunol. response in host)

L7 ANSWER 47 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:210 HCAPLUS

DOCUMENT NUMBER: 126:29069

TITLE: Cloning and characterization of the Helicobacter  
pylori cagI region 5' to the cagA gene and its  
therapeutic uses

INVENTOR(S): Covacci, Antonello

PATENT ASSIGNEE(S): Biocine S.P.A., Italy

SOURCE: PCT Int. Appl., 305 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633274	A1	19961024	WO 1996-IB343	19960418
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML			
US 5928865	A	19990727	US 1995-477451	19950607
AU 9651605	A1	19961107	AU 1996-51605	19960418
EP 821735	A1	19980204	EP 1996-908300	19960418
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 11506905	T2	19990622	JP 1996-531592	19960418
PRIORITY APPLN. INFO.:			US 1995-425194	A 19950420
			US 1995-477451	A 19950607
			IT 1992-FI52	A 19920302
			US 1995-471491	A2 19950606
			WO 1996-IB343	W 19960418

AB Helicobacter pylori is known to cause or be a cofactor in type B  
**gastritis**, **peptic ulcers**, and **gastric** tumors.

In both developed and developing countries, a high percentage of people  
are infected with this bacterium. The present invention relates generally  
to a certain H. pylori region located 5' to the CagA gene locus, to  
proteins encoded thereby, and to the use of these genes and proteins for  
diagnostic and **vaccine** applications. This region is present in  
type I H. pylori but absent from type II and appears to play a role in  
virulence.

IT **184491-43-8**, Protein (Helicobacter pylori gene cagA)

**184491-44-9 184539-26-2**

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; cloning and characterization of Helicobacter  
pylori cagI region 5' to cagA gene and its therapeutic uses)

IT **184539-25-1 184539-27-3 184539-28-4**  
**184539-29-5 184539-30-8 184539-31-9**  
**184539-32-0 184539-33-1 184539-34-2**  
**184539-35-3 184594-41-0 184594-42-1**  
**184594-43-2 184594-44-3 184594-45-4**  
**184594-46-5 184594-47-6 184594-48-7**

Searched by Mona Smith

184594-49-8 184594-50-1 184594-51-2  
 184594-52-3 184594-53-4 184594-54-5  
 184594-55-6 184594-56-7 184594-57-8  
 184594-58-9 184594-59-0 184594-60-3  
 184594-61-4 184594-62-5 184594-63-6  
 184594-64-7 184594-65-8 184594-66-9  
 184594-67-0 184594-68-1 184594-69-2  
 184594-70-5

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nucleotide sequence; cloning and characterization of *Helicobacter*  
*pylori* *cagI* region 5' to *cagA* gene and its therapeutic uses)

L7 ANSWER 48 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:740354 HCAPLUS

DOCUMENT NUMBER: 126:6446

TITLE: Protective *Helicobacter* antigens

INVENTOR(S): Doidge, Christopher Vincent; Lee, Adrian; Radcliff,  
 Fiona Jane; Hocking, Dianna Margaret; Webb, Elizabeth  
 Ann

PATENT ASSIGNEE(S): Csl Ltd., Australia

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633220	A1	19961024	WO 1996-AU225	19960419
W: AU, CA, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2217496	AA	19961024	CA 1996-2217496	19960419
AU 9652621	A1	19961107	AU 1996-52621	19960419
AU 693679	B2	19980702		
ZA 9603133	A	19970709	ZA 1996-3133	19960419
EP 821698	A1	19980204	EP 1996-908930	19960419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11504206	T2	19990420	JP 1996-531353	19960419
PRIORITY APPLN. INFO.:			AU 1995-2575	A 19950421
			AU 1995-3931	A 19950703
			AU 1996-7565	A 19960116
			WO 1996-AU225	W 19960419

AB Protective *Helicobacter* antigens, esp. *H. pylori* antigens, and the use of  
 these antigens as **vaccines** for the treatment or prevention of  
**gastroduodenal** disease assocd. with *H. pylori* infection. Mol.  
 cloning of *H. pylori* antigens or proteins was performed, and recombinant  
*H. pylori* antigens (i.e. 13, 17, 19, 29, 36 and 50 kDa) were cloned.  
 subcloned, expressed, purified, and tested in mouse model.

IT 9002-13-5, Urease

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(*Helicobacter*; recombinant *Helicobacter pylori* or *felis* antigens as  
**vaccine** for **gastroduodenal** disease)

IT 184050-44-0 184050-46-2 184050-48-4

184050-50-8 184050-51-9

RL: PRP (Properties)

(amino acid sequence; cDNA sequences for *Helicobacter pylori* antigens)

in relation to **vaccine** for **gastroduodenal** disease)  
IT 184050-43-9 184050-45-1 184050-47-3  
184050-49-5 184050-56-4  
RL: PRP (Properties)  
(nucleotide sequence; cDNA sequences for *Helicobacter pylori* antigens  
in relation to **vaccine** for **gastroduodenal** disease)

L7 ANSWER 49 OF 63 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:731124 HCAPLUS  
DOCUMENT NUMBER: 126:70729  
TITLE: Immunomagnetic bead enrichment and PCR for detection  
of *Helicobacter pylori* in human stools  
AUTHOR(S): Nilsson, Hans-Olof; Almljun, Paer; Nilsson, Ingrid;  
Tyszkiewicz, Tadeusz; Wadstroem, Torkel  
CORPORATE SOURCE: Department of Medical Microbiology, University of  
Lund, Soelvegatan 23, S-223 62, Lund, Swed.  
SOURCE: Journal of Microbiological Methods (1996), 27(1),  
73-79  
CODEN: JMIMDQ; ISSN: 0167-7012  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB An immunomagnetic bead-based polymerase chain reaction assay (IMS-PCR) was developed for the detection of *Helicobacter pylori* in exptl. inoculated human stools and human clin. stool samples. Magnetic beads coated with anti-*H. pylori* rabbit antibodies were used for enrichment and concn. of *H. pylori* from fecal samples. Taq polymerase inhibitors, found in human feces, are efficiently removed by the immunomagnetic sepn. (IMS) and subsequent washing of the magnetic beads. Conditions of the assay were developed and optimized with feces from a healthy, *H. pylori* seroneg., individual. Feces was inoculated with serial dilns. of either the spiral or the coccoid form of *H. pylori*. These 2 morphol. forms could be detected at similar concns. when inoculated in feces using an optimized IMS-PCR method. In 1 g of feces less than 2.5 .times. 10<sup>4</sup> *H. pylori* cells were detected as measured with 2 sep. sets of PCR-primers, based on a urease A subunit gene sequence and a gene sequence encoding a 26-kDa surface protein of *H. pylori*. Previously, no report has shown a sensitivity below 10<sup>6</sup> *H. pylori* in feces PCR. Preliminary anal. of stool samples from 17 patients with symptoms of **gastritis** and esophagitis by IMS-PCR showed a good correlation with EIA-anal. of *H. pylori* serum-antibodies from these patients. The results indicate that *H. pylori* cells are shed in feces of infected patients and that immunomagnetic bead PCR might be an appropriate method for clin. diagnosis and studies involving immunoprophylaxis, antibiotic treatment, as well as **vaccine** candidates.

IT 9002-13-5, Urease  
RL: MSC (Miscellaneous)  
(A, PCR primers based on gene for; immunomagnetic bead enrichment and PCR for detection of *Helicobacter pylori* in human stools)

L7 ANSWER 50 OF 63 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:121144 HCAPLUS  
DOCUMENT NUMBER: 124:168822  
TITLE: *Helicobacter pylori* nickel-binding protein sequence, gene, and potential use in **vaccination**, **ulcer** or cancer therapy, and environmental nickel removal  
INVENTOR(S): Plaut, Andrew G.; Gilbert-Rothstein, Joanne V.; Wright, Andrew  
PATENT ASSIGNEE(S): New England Medical Center Hospitals, Inc., USA;

Minnifield 09/955,739

SOURCE: Trustees of Tufts College  
PCT Int. Appl., 32 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533767	A1	19951214	WO 1995-US5772	19950509
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5780040	A	19980714	US 1994-255457	19940608
CA 2192312	AA	19951214	CA 1995-2192312	19950509
EP 770092	A1	19970502	EP 1995-919083	19950509
R: AT, CH, DE, FR, GB, LI				
JP 10506521	T2	19980630	JP 1995-500888	19950509
US 5972348	A	19991026	US 1998-115032	19980714
PRIORITY APPLN. INFO.:			US 1994-255457	19940608
			WO 1995-US5772	19950509
AB	The application discloses a nickel-binding protein and its encoding DNA isolated from <i>Helicobacter pylori</i> . This organism is the primary cause of chronic <b>gastritis</b> and ensuing peptic <b>ulcers</b> , and has been implicated in stomach cancer. The nickel-binding protein is useful to inhibit assembly of active ureases, the enzymes responsible for the pathogenic features of the bacterium. Potential uses include as a <b>vaccine</b> a diagnostic, a drug target, and a therapy in itself.			
IT	<b>169149-23-9</b> RL: ANT (Analyte); NUU (Other use, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (amino acid sequence; <i>Helicobacter pylori</i> nickel-binding protein sequence, gene, and potential use in <b>vaccination</b> , <b>ulcer</b> or cancer therapy, and environmental nickel removal)			
IT	<b>9002-13-5</b> , Urease RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (nickel-dependent subunit assembly inhibition; <i>Helicobacter pylori</i> nickel-binding protein sequence, gene, and potential use in <b>vaccination</b> , <b>ulcer</b> or cancer therapy, and environmental nickel removal)			
IT	<b>173763-86-5</b> RL: NUU (Other use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nucleotide sequence of; <i>Helicobacter pylori</i> nickel-binding protein sequence, gene, and potential use in <b>vaccination</b> , <b>ulcer</b> or cancer therapy, and environmental nickel removal)			

L7 ANSWER 51 OF 63 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1995:913485 HCAPLUS  
DOCUMENT NUMBER: 123:312246  
TITLE: *Helicobacter pylori* vacuolating toxin gene product useful for immunization  
INVENTOR(S): Cover, Timothy L.; Blaser, Martin J.  
PATENT ASSIGNEE(S): Vanderbilt Univ., USA  
SOURCE: PCT Int. Appl., 63 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522988	A1	19950831	WO 1995-US2219	19950223
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5721349	A	19980224	US 1994-200232	19940223
AU 9519274	A1	19950911	AU 1995-19274	19950223
EP 749322	A1	19961227	EP 1995-911868	19950223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09512703	T2	19971222	JP 1995-522437	19950223
PRIORITY APPLN. INFO.:				
			US 1994-200232	19940223
			US 1992-841644	19920226
			WO 1995-US2219	19950223
AB	Helicobacter pylori is the major causative agent of chronic superficial <b>gastritis</b> in humans and is assocd. with the pathogenesis of peptic <b>ulcer</b> disease and possibly <b>gastric</b> cancer. The Helicobacter pylori vacuolating toxin gene was cloned and sequenced and the protein purified. An immunogenic amt. of a protein in a pharmaceutically acceptable carrier is described providing immunization against H. pylori infection. In addn., nucleic acids that selectively hybridize with the vacuolating toxin encoding gene are described for identification. Lastly, a genetically altered mutant strain of H. pylori that does not express a functional vacuolating toxin is presented.			
IT	<b>155981-96-7P 155981-97-8P</b> RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (amino acid sequence; helicobacter pylori vacuolating toxin gene product useful for immunization)			
IT	<b>154681-04-6P 170213-64-6P</b> RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (nucleotide sequence; helicobacter pylori vacuolating toxin gene product useful for immunization)			
L7	ANSWER 52 OF 63 HCAPLUS COPYRIGHT 2002 ACS			
ACCESSION NUMBER:	1995:852008 HCAPLUS			
DOCUMENT NUMBER:	123:237791			
TITLE:	Urease-based <b>vaccine</b> and treatment for Helicobacter infection			
INVENTOR(S):	Michetti, Pierre; Cortesey-Theulaz, Irene; Blum, Andre; Davin, Catherine; Haas, Rainer; Kraehenbuhl, Jean-Pierre; Saraga, Emilia			
PATENT ASSIGNEE(S):	Oravax, Inc., USA			
SOURCE:	PCT Int. Appl., 114 pp. CODEN: PIXXD2			
DOCUMENT TYPE:	Patent			
LANGUAGE:	English			
FAMILY ACC. NUM. COUNT:	4			
PATENT INFORMATION:				
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522987	A1	19950831	WO 1995-US2202	19950223

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W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI,  
GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG,  
MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,  
TT, UA

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,  
LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,  
SN, TD, TG

US 6290962 B1 20010918 US 1994-200346 19940223

AU 9519681 A1 19950911 AU 1995-19681 19950223

AU 694195 B2 19980716

EP 751786 A1 19970108 EP 1995-912583 19950223

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

BR 9506884 A 19970819 BR 1995-6884 19950223

JP 09509661 T2 19970930 JP 1995-522429 19950223

PL 179149 B1 20000731 PL 1995-316007 19950223

NO 9603508 A 19961021 NO 1996-3508 19960822

FI 9603281 A 19961022 FI 1996-3281 19960822

PRIORITY APPLN. INFO.:

US 1994-200346 A 19940223

US 1992-970996 B2 19921103

US 1993-85938 A2 19930706

WO 1995-US2202 W 19950223

AB A method of eliciting in a mammalian host a protective immune response to  
Helicobacter infection and treatment of Helicobacter infection by  
administering to the host an immunogenically effective amt. of a  
**Helicobacter urease** or urease subunits as antigen is  
described. **Vaccine** compns. are also provided.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(urease-based **vaccine** and treatment for Helicobacter  
infection)

L7 ANSWER 53 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:772761 HCAPLUS

DOCUMENT NUMBER: 123:167618

TITLE: Immunogenic compositions against Helicobacter  
infection, polypeptides for use in the compositions  
and nucleic acid sequences encoding said polypeptides

INVENTOR(S): Labigne, Agnes; Suerbaum, Sebastien; Ferrero, Richard  
PATENT ASSIGNEE(S): Institut Pasteur, Fr.; Institut National de la Sante  
et de la Recherche Medicale (INSERM)

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514093	A1	19950526	WO 1993-EP3259	19931119
W: JP				
CA 2144307	AA	19941124	CA 1994-2144307	19940519
WO 9426901	A1	19941124	WO 1994-EP1625	19940519
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9469290	A1	19941212	AU 1994-69290	19940519
AU 689779	B2	19980409		
EP 703981	A1	19960403	EP 1994-917653	19940519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

Searched by Mona Smith

Minnifield 09/955,739

JP 08510120	T2	19961029	JP 1994-524997	19940519
US 6248330	B1	20010619	US 1995-432697	19950502
US 5843460	A	19981201	US 1995-467822	19950606
US 6258359	B1	20010710	US 1995-466248	19950606
AU 9875081	A1	19981001	AU 1998-75081	19980709
AU 724584	B2	20000928		

PRIORITY APPLN. INFO.:

EP 1993-401309	A	19930519
WO 1993-EP3259	A	19931119
WO 1994-EP1625	W	19940519
US 1995-432697	A2	19950502
US 1995-447177	A1	19950519

AB The invention relates to an immunogenic compn., capable of inducing protective antibodies against *Helicobacter* infection, characterized in that it comprises: i) at least one subunit of a urease structural polypeptide from *Helicobacter pylori*, or a fragment thereof, said fragment being recognized by antibodies reacting with *Helicobacter felis* urease, and/or at least one subunit of a urease structural polypeptide from *Helicobacter felis*, or a fragment thereof, said fragment being recognized by antibodies reacting with *Helicobacter pylori* urease; ii) optionally, a urease-assocd. Heat Shock protein (HSP), or chaperonin, from *Helicobacter*, or a fragment of said protein.

IT **151187-40-5P**, Urease (*Helicobacter felis* strain ATCC 49179 gene ureB .beta.-6 subunit reduced) **162243-38-1P 162243-40-5P**, Urease (*Helicobacter felis* gene ureA) **162243-42-7P**, Urease (*Helicobacter felis* gene ureI) **167293-79-0P**  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence of; immunogenic compns. against *Helicobacter* infection, polypeptides for use in compns. and nucleic acid sequences encoding said polypeptides)

IT **162243-39-2 162243-43-8**, Deoxyribonucleic acid (*Helicobacter felis* gene ureI) **167293-74-5 167293-75-6 167293-76-7 167293-77-8 167293-78-9**  
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(nucleotide sequence of; immunogenic compns. against *Helicobacter* infection, polypeptides for use in compns. and nucleic acid sequences encoding said polypeptides)

IT **9002-13-5P**, Urease  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(subunit A and subunit B; immunogenic compns. against *Helicobacter* infection, polypeptides for use in compns. and nucleic acid sequences encoding said polypeptides)

L7 ANSWER 54 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:702389 HCAPLUS

DOCUMENT NUMBER: 123:167008

TITLE: Oral immunization with recombinant *Helicobacter pylori* urease induces secretory IgA antibodies and protects mice from challenge with *Helicobacter felis*

AUTHOR(S): Lee, Cynthia K.; Weltzin, Richard; Thomas, William D.; Kleanthous, Harold; Ermak, Thomas H.; Soman, Gopalan; Hill, Joseph E.; Ackerman, Samuel K.; Monath, Thomas P.

CORPORATE SOURCE: OraVax Inc., Cambridge, MA, 02139, USA

SOURCE: J. Infect. Dis. (1995), 172(1), 161-72

CODEN: JIDIAQ; ISSN: 0022-1899

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *Helicobacter pylori*, a gram-neg. spiral bacterium, is the cause of chronic superficial (type B) **gastritis** and peptic ulcer disease. The urease enzyme of *H. pylori* was expressed as an inactive recombinant protein in *Escherichia coli*, purified as particulate structures of 550-600 kDa mol. mass with a diam. of .apprx. 12 nm. Given orally, 5 .mu.g of urease with an appropriate mucosal adjuvant, such as the labile toxin of *E. coli*, protected 60%-100% of mice against challenge with virulent *Helicobacter felis*. Protection correlated with the level of secretory IgA antibodies against urease. Oral administration of antigen was as effective or better than **intragastric** administration. Parenteral injection of antigen or **intragastric** administration of high-dose antigen without adjuvant elicited serum IgG but no IgA antibodies and did not confer protection. Recombinant urease as an oral **vaccine** candidate deserves further investigation as an approach to the prevention of *Helicobacter*-induced chronic **gastroduodenal** diseases in humans.

IT 9002-13-5, Urease

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oral immunization with recombinant *Helicobacter pylori* urease induces secretory IgA and protects mice from challenge with *H. felis*)

L7 ANSWER 55 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:676998 HCAPLUS

DOCUMENT NUMBER: 123:81196

TITLE: The GroES homolog of *Helicobacter pylori* confers protective immunity against mucosal infection in mice  
AUTHOR(S): Ferrero, Richard L.; Thiberge, Jean-Michel; Kansau, Imad; Wuscher, Nicole; Huerre, Michel; Labigne, Agnes  
CORPORATE SOURCE: Unite Enterobacteries, Inst. Natl. Sante Rech. Med. U389, Paris, 75724, Fr.

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1995), 92(14), 6499-503

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *Helicobacter pylori* is an important etiol. agent of **gastroduodenal** disease. In common with other organisms, *H. pylori* bacteria express heat shock proteins that share homologies with the GroES-GroEL class of proteins from *Escherichia coli*. The authors have assessed the heat shock proteins of *H. pylori* as potential protective antigens in a murine model of **gastric** *Helicobacter* infection. **Orogastric** immunization of mice with recombinant *H. pylori* GroES- and GroEL-like proteins protected 80% and 70% of animals, resp., from a challenge dose of 104 *Helicobacter felis* bacteria (compared to control mice, and, resp.). All mice that were immunized with a dual antigen prep., consisting of *H. pylori* GroES-like protein and the B subunit of *H. pylori* urease, were protected against infection. This represented a level of protection equiv. to that provided by a sonicated *Helicobacter* ext. Antibodies directed against the recombinant *H. pylori* antigens were predominantly of the IgG1 class, suggesting that a type 2 T-helper cell response was involved in protection. This work reports a protein belonging to the GroES class of heat shock proteins that was shown to induce protective immunity. In conclusion, GroES-like and urease B-subunit proteins have been identified as potential components of a future *H. pylori* subunit **vaccine**.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(protective immunity against *Helicobacter pylori* mucosal infection is induced by HspA protein and B subunit of)



L7 ANSWER 56 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:634741 HCAPLUS  
 DOCUMENT NUMBER: 123:17850  
 TITLE: Oral **vaccines** containing urease antigen for prevention or treatment of Helicobacter infections  
 INVENTOR(S): Leveen, Harry H.; Laveen, Eric G.; Laveen, Robert F.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: Eur. Pat. Appl., 12 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 654273	A1	19950524	EP 1994-308551	19941118
R: DE, FR, GB, IT				
PRIORITY APPLN. INFO.:			US 1993-153856	19931118
			US 1993-153857	19931118
			US 1994-185749	19940124

AB Oral **vaccines** contg. a non-enzymic urease antigen for treating and/or preventing Helicobacter infections. Acid urease was obtained from culture of lactobacillus fermentum and was reacted with glutaraldehyde to form a non-enzymic urease antigen. Mice were immunized with the inactive urease antigen prior to the challenging dose of Helicobacter felis were protected from development of **gastritis**. The infecting organism could not be recovered from the **gastric** content and was not present on histol. examn. of **gastric** tissue.

IT **9002-13-5**, Urease  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antigen; oral **vaccines** contg. urease antigen for prevention or treatment of Helicobacter infections)

L7 ANSWER 57 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:467429 HCAPLUS  
 DOCUMENT NUMBER: 122:237257  
 TITLE: Effect of oral immunization with recombinant urease on murine Helicobacter felis **gastritis**  
 AUTHOR(S): Pappo, J.; Thomas, W. D., Jr.; Kabok, Z.; Taylor, N. S.; Murphy, J. C.; Fox, J. G.  
 CORPORATE SOURCE: Vaccine Delivery Res. Microbiol. Sections, Massachusetts Inst. Technol., Cambridge, MA, 02139, USA  
 SOURCE: Infect. Immun. (1995), 63(4), 1246-52  
 CODEN: INFIBR; ISSN: 0019-9567  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The ability of oral immunization to interfere with the establishment of infection with Helicobacter felis was examd. Groups of Swiss Webster mice were immunized orally with 250 .mu.g of Helicobacter pylori recombinant urease (rUrease) and 10 .mu.g of cholera toxin (CT) adjuvant, 1 mg of H. felis sonicate antigens and CT, or phosphate-buffered saline (PBS) and CT. Oral immunization with rUrease resulted in markedly elevated serum IgG (IgG), serum IgA, and intestinal IgA antibody responses. Challenge with live H. felis further stimulated the urease-specific intestinal IgA and serum IgG and IgA antibody levels in mice previously immunized with rUrease but activated primarily the serum IgG compartment of PBS-treated and H. felis-immunized mice. Intestinal IgA and serum IgG and IgA

anti-urease antibody responses were highest in rUrease-immunized mice at the termination of the expt. Mice immunized with rUrease were significantly protected against infection when challenged with *H. felis* 2 or 6 wk post-oral immunization in comparison with PBS-treated mice. Whereas *H. felis*-infected mice displayed multifocal **gastric** mucosal lymphoid follicles consisting of CD45R+ B cells surrounded by clusters of Thyl.2+ T cells, **gastric** tissue from rUrease-immunized mice contained few CD45R+ B cells and infrequent mucosal follicles. These observations show that oral immunization with rUrease confers protection against *H. felis* infection and suggest that **gastric** tissue may function as an effector organ of the mucosal immune system which reflects the extent of local antigenic stimulation.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(effect of oral immunization with recombinant urease on murine *Helicobacter felis* **gastritis** and Ig levels)

L7 ANSWER 58 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:442082 HCAPLUS  
DOCUMENT NUMBER: 122:236681  
TITLE: Development of a mouse model of *Helicobacter pylori* infection that mimics human disease  
AUTHOR(S): Marchetti, Marta; Arico, Beatrice; Burroni, Daniela; Figura, Natale; Rappuoli, Rino; Ghiara, Paolo  
CORPORATE SOURCE: IRIS, Biocine SpA, Siena, 53100, Italy  
SOURCE: Science (Washington, D. C.) (1995), 267(5204), 1655-8  
CODEN: SCIEAS; ISSN: 0036-8075  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The human pathogen *Helicobacter pylori* is assocd. with **gastritis**, peptic **ulcer** disease, and **gastric** cancer. The pathogenesis of *H. pylori* infection in vivo was studied by adapting fresh clin. isolates of bacteria to colonize the stomachs of mice. A **gastric** pathol. resembling human disease was obsd. in infections with cytotoxin-producing strains but not with noncytotoxic strains. Oral immunization with purified *H. pylori* antigens protected mice from bacterial infection. This mouse model will allow the development of therapeutic agents and **vaccines** against *H. pylori* infection in humans.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(protection from *Helicobacter pylori* infection of mouse by immunization using)

L7 ANSWER 59 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:698698 HCAPLUS  
DOCUMENT NUMBER: 121:298698  
TITLE: Recombinant antigens prepared from the urease subunits of *Helicobacter* spp.: evidence of protection in a mouse model of **gastric** infection  
AUTHOR(S): Ferrero, Richard L.; Thiberge, Jean-Michel; Huerre, Michel; Labigne, Agnes  
CORPORATE SOURCE: Unite Enterobacteries, Inst. Pasteur, Paris, 75724, Fr.  
SOURCE: Infect. Immun. (1994), 62(11), 4981-9  
CODEN: INFIBR; ISSN: 0019-9567  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Urease is an important virulence factor for **gastric** *Helicobacter* spp. To elucidate the efficacy of individual urease subunits to act as mucosal immunogens, the genes encoding the resp. urease subunits (UreA and UreB) of *Helicobacter pylori* and *Helicobacter felis* were cloned in an expression vector (pMAL) and expressed in *Escherichia coli* cells as translational fusion proteins. The recombinant UreA and UreB proteins were purified by affinity and anion-exchange chromatog. techniques and had predicted mol. masses of approx. 68 to 103 kDa, resp. Western blotting (immunoblotting) studies indicated that the urease components of the fusion proteins were strongly immunogenic and were specifically recognized by polyclonal rabbit anti-*Helicobacter* sp. sera. The fusion proteins (50 .mu.g) were used, in combination with a mucosal adjuvant (cholera toxin), to **orogastrically** immunize mice against *H. felis* infection. **Gastric** tissues from *H. felis*-challenged mice were assessed by the biopsy urease test and by histol. In mice immunized with recombinant *H. felis* UreB, 60% of animals (n = 7) were histol. neg. for *H. felis* bacteria after challenge at 17 wk. This compared with 25% (n = 8) for mice immunized with the heterologous *H. pylori* UreB antigen. Neither the homologous nor the heterologous UreA subunit elicited protective responses against *H. felis* infection in mice. The study demonstrated that a recombinant subunit antigen could induce an immunoprotective response against **gastric** *Helicobacter* infection.

IT 9002-13-5, Urease

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(recombinant urease subunits induce protective immunity against *Helicobacter* species)

L7 ANSWER 60 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:291205 HCAPLUS

DOCUMENT NUMBER: 120:291205

TITLE: Gene Structure of the *Helicobacter pylori* Cytotoxin and Evidence of Its Key Role in **Gastric** Disease

AUTHOR(S): Telford, John L.; Ghiara, Paolo; Dell'Orco, Mariangela; Comanducci, Maurizio; Burroni, Daniela; Bugnoli, Massimo; Tecce, Mario F.; Censini, Stefano; Covacci, Antonello; et al.

CORPORATE SOURCE: Dep. Mol. Biol., Res. Inst. Siena, Siena, 53100, Italy

SOURCE: J. Exp. Med. (1994), 179(5), 1653-8

CODEN: JEMEAV; ISSN: 0022-1007

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The gram neg., microaerophilic bacterium *Helicobacter pylori* colonizes the human **gastric** mucosa and establishes a chronic infection that is tightly assocd. with atrophic **gastritis**, peptic **ulcer**, and **gastric** carcinoma. Cloning of the *H. pylori* cytotoxin gene shows that the protein is synthesized as a 140-kD precursor that is processed to a 94-kD fully active toxin. Oral administration to mice of the purified 94-kD protein caused **ulceration** and **gastric** lesions that bear some similarities to the pathol. obsd. in humans. The cloning of the cytotoxin gene and the development of a mouse model of human **gastric** disease will provide the basis for the understanding of *H. pylori* pathogenesis and the development of therapeutics and **vaccines**.

IT 154984-93-7, Cytotoxin (*Helicobacter pylori* precursor)

RL: PRP (Properties)

(amino acid sequence of and **ulceration** and **gastric** lesions induced in mice by)

IT 154984-92-6, DNA (*Helicobacter pylori* cytotoxin gene plus flanks)

RL: PRP (Properties); BIOL (Biological study)  
(nucleotide sequence of)

L7 ANSWER 61 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:2256 HCAPLUS

DOCUMENT NUMBER: 120:2256

TITLE: Helicobacter pylori proteins useful for  
**vaccines** and diagnostics

INVENTOR(S): Covacci, Antonello; Bugnoli, Massimo; Telford, John;  
Macchia, Giovanni; Rappuoli, Rino

PATENT ASSIGNEE(S): Biocine Sclavo S.p.A., Italy

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9318150	A1	19930916	WO 1993-EP472	19930302
W:	AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG			
AU 9336300	A1	19931005	AU 1993-36300	19930302
EP 643770	A1	19950322	EP 1993-905285	19930302
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
JP 07504565	T2	19950525	JP 1993-515309	19930302
EP 967279	A1	19991229	EP 1999-202698	19930302
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE			
JP 2000333686	A2	20001205	JP 2000-126696	19930302
JP 2000350591	A2	20001219	JP 2000-126695	19930302
US 6077706	A	20000620	US 1995-470260	19950606
US 6130059	A	20001010	US 1995-466662	19950606
PRIORITY APPLN. INFO.:			IT 1992-FI52	A 19920302
			WO 1993-EP158	A 19930125
			EP 1993-905285	A3 19930302
			JP 1993-515309	A 19930302
			WO 1993-EP472	A 19930302
			US 1994-256848	B3 19941021
AB	The H. pylori genes for cytotoxin, CAI (cytotoxin-assocd. immunodominant) antigen, and heat-shock protein (of the hsp60 family) are cloned and sequenced. The nucleic acids and proteins may be used for diagnosis and the proteins for <b>vaccination</b> against H. pylori. The cytotoxin, or CT antigen, gene encoded a 140 kDa protein precursor of a 100 kDa protein with urease-independent vacuolating activity. The CAI antigen gene was absent in noncytotoxic H. pylori strains. The heterogeneity of the CAI antigen appeared to be due to internal duplications in the gene: strain G39 was found to have two identical repeats of a 102 bp sequence within the gene. The heat-shock protein gene was expressed in all H. pylori strains tested, both cytotoxic and noncytotoxic. Most sera from patients infected with H. pylori and exhibiting <b>gastritis</b> and <b>ulcers</b> contained antibodies to the hsp, but the degree of recognition varied greatly among the patients and the antibody levels did not show any obvious correlation with the type of disease.			
IT	151354-79-9, CAI antigen (Helicobacter pylori strain CCUG 17874 clone A1) 151441-76-8, Heat-shock protein (Helicobacter pylori clone pHp60G5) 151639-33-7, Cytotoxin (Helicobacter pylori clone			

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TOXEE1 precursor) 151639-36-0, CAI antigen (Helicobacter pylori strain G39)

RL: PRP (Properties)

(amino acid sequence of)

IT 149738-23-8, DNA (Helicobacter pylori strain CCUG 17874 clone A1 CAI antigen gene and flanks) 151243-14-0, DNA (Helicobacter pylori clone pHp60G5 heat-shock protein gene and flanks) 151639-32-6, DNA (Helicobacter pylori clone TOXEE1 cytotoxin gene and flanks) 151639-35-9, DNA (Helicobacter pylori strain G39 CAI antigen gene and flanks)

RL: PRP (Properties); BIOL (Biological study)

(nucleotide sequence of)

L7 ANSWER 62 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:664549 HCAPLUS

DOCUMENT NUMBER: 119:264549

TITLE: Purified vacuolating toxin from Helicobacter pylori and its use in diagnosis and **vaccines**

INVENTOR(S): Cover, Timothy L.; Blaser, Martin J.

PATENT ASSIGNEE(S): Vanderbilt University, USA

SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9316723	A1	19930902	WO 1993-US1558	19930224	
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG					
AU 9337282	A1	19930913	AU 1993-37282	19930224	
EP 629132	A1	19941221	EP 1993-906142	19930224	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 07507444	T2	19950824	JP 1993-515007	19930224	
US 6054132	A	20000425	US 1994-284747	19940802	
US 5859219	A	19990112	US 1994-295643	19941027	
US 6013463	A	20000111	US 1995-473265	19950607	
PRIORITY APPLN. INFO.:				US 1992-841644	19920226
				WO 1993-US1558	19930224
				US 1994-284747	19940802

AB H. pylori, a causative agent of chronic **gastritis**, produces a toxin (CB antigen) which can be used as a basis for **vaccines** and for producing antibodies for diagnostic tests. The toxin, purified chromatog. from H. pylori, had an N-terminal amino acid sequence partially homologous to those of various ion channel proteins and permeases. Portions of the toxin gene were amplified by PCR, cloned, and sequenced. A neutralizing antiserum to the toxin was produced in rabbits and used for detection of the toxin. An ELISA is described for detection of anti-toxin antibodies in human serum for diagnosis of infection with toxigenic H. pylori. Cellular damage (vacuolation) from the toxin was prevented in HeLa cells by bafilomycin A1, an inhibitor of vacuolar-type ATPase.

IT 151441-14-4

RL: PRP (Properties); BIOL (Biological study)

(nucleotide sequence and cloning of)

L7 ANSWER 63 OF 63 HCAPLUS COPYRIGHT 2002 ACS

Searched by Mona Smith

Minnifield 09/955,739

ACCESSION NUMBER: 1991:651669 HCAPLUS  
DOCUMENT NUMBER: 115:251669  
TITLE: A method for the stepwise, controlled synthesis of chemical species, particularly peptides, on protein substrates, coupled products obtained by the method, and the use of these coupled products, e.g. as **vaccines**  
INVENTOR(S): Houen, Gunnar; Holm, Arne  
PATENT ASSIGNEE(S): Den.  
SOURCE: PCT Int. Appl., 106 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9108220	A1	19910613	WO 1990-DK311	19901130
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, GR, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9168929	A1	19910626	AU 1991-68929	19901130
PRIORITY APPLN. INFO.:			DK 1989-6085	19891201
			WO 1990-DK311	19901130

AB Chem. species, esp. peptides, are synthesized by a stepwise, controlled process using a proteinaceous substances as the synthesis substrate. The coupled products obtained by the process can be used, e.g., as **vaccines**, matrix materials, or carrier mols. The products, including peptides and peptide derivs., prepd. by the method are also claimed. Bovine serum albumin (BSA) was placed in a silylated reaction vessel and the CO<sub>2</sub>H groups were diethylamidated before coupling glutamic acid as the Fmoc (9-fluorenylmethyloxycarbonyl) and tert-Bu protected Dhbt (3-hydroxy-3,4-dihydrobenzotriazin-4-one ester, blocking remaining amino groups with acetic anhydride, and sequentially coupling Fmoc- and side chain-protected Dhbt esters of lysine, serine, threonine, aspartic acid, methionine, and serine. Piperidine was used to remove the Fmoc protecting group between couplings. Side chain protection groups were removed in CH<sub>2</sub>Cl<sub>2</sub>/F<sub>3</sub>CCO<sub>2</sub>H (1:1 vol./vol.) at 0.degree.. The product had an av. of 35 synthesized peptide chains per BSA mol. The coupled product was used to raise antibodies to Ser-Met-Asp-Thr-Ser-Lys-Glu in rabbits.

IT **9002-13-5**, Urease  
RL: ANST (Analytical study)  
(as carrier for peptide synthesis)

show files

File 155:MEDLINE(R) 1966-2002/Jul W2  
 File 5:Biosis Previews(R) 1969-2002/Jul W2  
     (c) 2002 BIOSIS  
 File 34:SciSearch(R) Cited Ref Sci 1990-2002/Jul W3  
     (c) 2002 Inst for Sci Info  
 File 35:Dissertation Abs Online 1861-2002/Jun  
     (c) 2002 ProQuest Info&Learning  
 File 50:CAB Abstracts 1972-2002/Jun  
     (c) 2002 CAB International  
 File 65:Inside Conferences 1993-2002/Jul W3  
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     (c) 2002 Cambridge Sci Abs  
 File 77:Conference Papers Index 1973-2002/Jul  
     (c) 2002 Cambridge Sci Abs  
 File 144:Pascal 1973-2002/Jul W3  
     (c) 2002 INIST/CNRS  
 File 162:CAB HEALTH 1983-2002/Jun  
     (c) 2002 CAB INTERNATIONAL  
 File 345:Inpadoc/Fam. & Legal Stat 1968-2002/UD=199970  
     (c) 2002 EPO  
 File 351:Derwent WPI 1963-2002/UD,UM &UP=200246  
     (c) 2002 Thomson Derwent  
 File 357:Derwent Biotech Res. 1982-2002/June W1  
     (c) 2002 Thomson Derwent & ISI  
 File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec  
     (c) 1998 Inst for Sci Info  
 File 440:Current Contents Search(R) 1990-2002/Jul 23  
     (c) 2002 Inst for Sci Info

?ds

Set	Items	Description
S1	731	(H OR HELICOBACTER?) (S)UREASE? AND VACCIN?
S2	258	RD (unique items)
S3	248	S2 AND (GASTR? OR ULCER? OR INTEST? OR STOMACH? OR METAPLA- SIA? OR LYMPHOMA? OR PYLORI OR FELIS)
S4	142	S2(S) (GASTRI? OR GASTRO? OR ULCER? OR INTESTIN? OR STOMACH? OR METAPLASIA? OR LYMPHOMA?)
S5	80	S4 AND PY=(2002 OR 2001 OR 1999 OR 1998 OR 1997)
S6	62	S4 NOT S5

?t6/3 ab/1-62

>>>No matching display code(s) found in file(s): 65, 345

6/AB/1 (Item 1 from file: 155)  
 DIALOG(R)File 155:MEDLINE(R)

10872412 20432624 PMID: 10974142  
 Quantitative and bioluminescent assay to measure efficacy of conventional  
 and DNA vaccinations against Helicobacter pylori.  
 Ozpolat B; Rao X M; Lachman L B; Osato M S; Graham D Y  
 Department of Bioimmunotherapy, University of Texas M. D. Anderson Cancer  
 Center, Houston, TX 77030, USA.  
 Combinatorial chemistry & high throughput screening (NETHERLANDS) Aug  
 2000, 3 (4) p289-302, ISSN 1386-2073 Journal Code: 9810948  
 Contract/Grant No.: CA16672; CA; NCI  
 Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Vaccination against *Helicobacter pylori* using DNA sequences encoding Urease A and B subunits was compared to immunization with urease antigen and MTP-PE in a liposome formulation. To determine the effectiveness of a vaccine against *H. pylori* in a mouse model it is essential to quantify the number of *H. pylori* remaining in the stomachs following challenge with an inoculum of live bacteria. Culture assays and enzymatic assays produce inconsistent results often unsuitable to conclude if vaccine candidates are protective. To overcome this problem, we developed two assays: 1) a competitive quantitative PCR using a colorimetric readout and 2) a non-competitive direct quantitative PCR using a highly sensitive bioluminescent readout. The competitive PCR requires coamplification of a segment of the urease C sequence and an internal control standard in a competitive manner using a single set of primers. PCR products were quantified colorimetrically by an enzyme-linked immunosorbent assay and compared with known quantities of the internal control standard added to the PCR reaction. The highly sensitive, bioluminescent assay measures the amplified DNA directly using a flash-type luminescent tag and a specific probe. The Sydney strain of *H. pylori* was used for the mouse infection model. Quantification of *H. pylori* by either the bioluminescent assay or the competitive PCR was reliable, specific and sensitive compared to quantitative growth assays which often gave false results. The bioluminescent assay was much more sensitive and less labor/time intensive than the competitive PCR. The bioluminescent assay was able to quantitate as few as 100 bacteria, while the competitive assay could not detect less than 10(3) bacteria per mouse stomach. Quantification of *H. pylori* by bioluminescent assay was superior to the competitive assay and may be used for research applications, such as the development of vaccines, pathogenesis of gastric disease and monitoring of antibiotic treatment.

6/AB/2 (Item 2 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10851595 20380106 PMID: 10926118

The mucosal adjuvanticity of two nontoxic mutants of *Escherichia coli* heat-labile enterotoxin varies with immunization routes.

Park E J; Chang J H; Kim J S; Yum J S; Chung S I

Mogam Biotechnology Research Institute, Yonginsu, Kyonggido, Korea.

Experimental & molecular medicine (KOREA (SOUTH)) Jun 30 2000, 32 (2)

p72-8, ISSN 1226-3613 Journal Code: 9607880

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

*Escherichia coli* heat-labile enterotoxin (LT), which causes a characteristic diarrhea in humans and animals, is a strong mucosal immunogen and has powerful mucosal adjuvant activity towards coadministered unrelated antigens. Here we report the different mucosal adjuvanticity of nontoxic LT derivatives, LTS63Y and LTdelta110/112, generated by immunizing through two different mucosal routes. Intragastric (IG) immunization with *Helicobacter pylori* urease alone resulted in poor systemic IgG and IgA responses and no detectable local secretory IgA, but IG co-immunization with urease and LTdelta110/112 induced high titers of urease-specific local secretory IgA and systemic IgG and IgA, comparable to those induced by wild-type LT. LTS63Y showed far lower adjuvant activity towards urease than LTdelta110/112 in IG immunization, but was more active than LTdelta110/112 in inducing immune responses to urease by intranasal (IN) immunization. LTdelta110/112 predominantly enhanced the induction of



urease -specific IgG1 levels following IG immunization; whereas LTS63Y induced high levels of IgG1, IgG2a and IgG2b following IN immunization. In addition, quantitative *H. pylori* culture of stomach tissue following challenge with *H. pylori* demonstrated a 90-95% reduction ( $p < 0.0002$ ) in bacterial burden in mice immunized intranasally with urease using either mutant LT as an adjuvant. These results indicate that the mechanism(s) underlying the adjuvant activities of mutant LTs towards coadministered *H. pylori* urease may differ between the IN and IG mucosal immunization routes.

6/AB/3 (Item 3 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10760102 20291464 PMID: 10828751

Challenges to therapy in the future.

O'Morain C; Montague S

Gastroenterology Department, Adelaide and Meath Hospital, Tallaght, Dublin, Ireland.

Helicobacter (UNITED STATES) 2000, 5 Suppl 1 pS23-6; discussion S27-31, ISSN 1083-4389 Journal Code: 9605411

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Quadruple therapy (with a proton pump inhibitor (PPI), metronidazole, tetracycline and bismuth) is generally reserved for second-line treatment; however, studies using this regimen for 7 days have found it to be effective even in metronidazole-resistant strains. Resistance is an ongoing problem with antimicrobial therapy but considerable progress has now been made into understanding the underlying genetic mechanisms of this process. Metronidazole resistance in Europe is usually in the range of 20-30% of strains but may be as high as 70% in some countries. One genetic mechanism involved is thought to be a mutation of the *rdxA* gene. Macrolide resistance appears to be on the increase in Europe, varying from 1% in some countries to 13% in others. The genetic mechanism involved has been shown to be a point mutation of a ribosomal RNA. Amoxicillin resistance is an emerging problem that has an adverse effect on eradication rates in clinical practice. Resistance has been shown to be caused by the absence of one of the four binding proteins in the cell wall. Few novel antibiotics have been developed for use in eradication therapy, although rifabutin, secnidazole and furazolidone have shown some success as part of combination therapy. Alternative therapies that have been tested include mucosal protective agents which have been used in place of a PPI in some eradication regimens with some success, and the somatostatin analog, octreotide, that has been used as part of quadruple therapy in place of a PPI and produced eradication rates of approximately 88%. The ultimate challenge is still to develop a safe and effective vaccine against *Helicobacter pylori*. Current and future research will also focus on identifying genetic targets for therapy, adhesion molecule analogs to prevent binding of the bacterium, and urease inhibitors. The current triple therapy treatment options available for the eradication of *Helicobacter pylori* infection are over 90% effective in susceptible organisms and there are very few medical conditions to which we can offer such efficacious treatment. Unfortunately, the recommendations made at consensus conferences are not always put into practice and physicians in primary care may be unaware of the true efficacy of eradication therapy. Treatment is very simple: three drugs, twice a day for 1 week. The main focus for both primary care physicians and gastroenterologists should be to reinforce the need for patient compliance, otherwise we will see an increase in antibiotic resistance. Patients should be prewarned that they may experience some mild side

effects and should be encouraged to complete the course of treatment. The real challenge for the future will be the management of patients who do not respond to first-line treatment. This paper will focus on potential problems with therapy, such as antibiotic resistance, and possible future solutions, such as novel antibiotics and vaccines.

6/AB/4 (Item 4 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10707114 20245734 PMID: 10781854

Further development of the *Helicobacter pylori* mouse vaccination model.  
Sutton P; Wilson J; Lee A  
School of Microbiology and Immunology, University of New South Wales,  
Sydney, Australia.

Vaccine (ENGLAND) Jun 1 2000, 18 (24) p2677-85, ISSN 0264-410X  
Journal Code: 8406899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Immunisation against *Helicobacter* infection in mouse models has thus far produced neither complete protection against the bacteria, nor a complete prevention of the associated gastritis. This study aimed firstly to compare the sensitivities of the various methods used to assess *H. pylori* infection in the mouse model, and secondly to develop the experimental design to induce a more effective immunity, aimed at further reducing bacterial burden in the gastric tissue. Various mouse strains were prophylactically immunised with whole bacterial sonicate and cholera toxin before challenge with *H. pylori*-SS1. The relative sensitivities of the urease assay, histological assessment and the colony forming assay to detect levels of *H. pylori* colonisation were compared. Comparisons of different antigen doses and different timecourses of immunisation were performed. The colony forming assay was found to be far more sensitive than either the urease assay or histological assessment for determining the protective efficacies of immunisation. Mice which had 10(5) *H. pylori* per gram of stomach by colony assay were negative by histology and urease. Lower doses of whole cell sonicate were more protective than high doses and more effective immunisation was achieved by leaving at least 3 weeks between immunisation instead of weekly immunisations. In conclusion, for assessment of *H. pylori* colonisation in the mouse model, the colony forming assay should be used. The experimental protocol for immunisation has been altered to produce a significant improvement in protection. However, full protection has still not yet been achieved and more work is still required.

6/AB/5 (Item 5 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10700293 20231817 PMID: 10768972

Parenteral adjuvant activities of *Escherichia coli* heat-labile toxin and its B subunit for immunization of mice against gastric *Helicobacter pylori* infection.

Weltzin R; Guy B; Thomas W D; Giannasca P J; Monath T P

OraVax, Inc., Cambridge, Massachusetts 02139, USA. rweltzin@oravax.com

Infection and immunity (UNITED STATES) May 2000, 68 (5) p2775-82,  
ISSN 0019-9567 Journal Code: 0246127

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The heat-labile toxin (LT) of *Escherichia coli* is a potent mucosal adjuvant that has been used to induce protective immunity against *Helicobacter felis* and *Helicobacter pylori* infection in mice. We studied whether recombinant LT or its B subunit (LTB) has adjuvant activity in mice when delivered with *H. pylori* urease antigen via the parenteral route. Mice were immunized subcutaneously or intradermally with urease plus LT, recombinant LTB, or a combination of LT and LTB prior to intragastric challenge with *H. pylori*. Control mice were immunized orally with urease plus LT, a regimen shown previously to protect against *H. pylori* gastric infection. Parenteral immunization using either LT or LTB as adjuvant protected mice against *H. pylori* challenge as effectively as oral immunization and enhanced urease-specific immunoglobulin G (IgG) responses in serum as effectively as aluminum hydroxide adjuvant. LT and LTB had adjuvant activity at subtoxic doses and induced more consistent antibody responses than those observed with oral immunization. A mixture of a low dose of LT and a high dose of LTB stimulated the highest levels of protection and specific IgG in serum. Urease-specific IgG1 and IgG2a antibody subclass responses were stimulated by all immunization regimens tested, but relative levels were dependent on the adjuvant used. Compared to parenteral immunization with urease alone, LT preferentially enhanced IgG1, while LTB or the LT-LTB mixture preferentially enhanced IgG2a. Parenteral immunization using LT or LTB as adjuvant also induced IgA to urease in the saliva of some mice. These results show that LT and LTB stimulate qualitatively different humoral immune responses to urease but are both effective parenteral adjuvants for immunization of mice against *H. pylori* infection.

6/AB/6 (Item 6 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10700265 20231789 PMID: 10768944

Immunization with recombinant *Helicobacter pylori* urease in specific-pathogen-free rhesus monkeys (*Macaca mulatta*).

Solnick J V; Canfield D R; Hansen L M; Torabian S Z  
Department of Internal Medicine (Division of Infectious Diseases),  
University of California, Davis School of Medicine, Davis, California  
95616, USA. jvsolnick@ucdavis.edu

Infection and immunity (UNITED STATES) May 2000, 68 (5) p2560-5,  
ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: AI-42081; AI; NIAID; RR00169; RR; NCRR

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Immunization with urease can protect mice from challenge with *Helicobacter pylori*, though results vary depending on the particular vaccine, challenge strain, and method of evaluation. Unlike mice, rhesus monkeys are naturally colonized with *H. pylori* and so may provide a better estimate of vaccine efficacy in humans. The purpose of this study was to examine the effectiveness of *H. pylori* urease as a vaccine in specific-pathogen (*H. pylori*)-free rhesus monkeys. Monkeys raised from birth and documented to be free of *H. pylori* were vaccinated with orogastric (n = 4) or intramuscular (n = 5) urease. Two control monkeys were sham vaccinated. All monkeys were challenged with a rhesus monkey-derived strain of *H. pylori*, and the effects of vaccination were evaluated by use of quantitative cultures of gastric tissue, histology, and measurement of serum immunoglobulin G (IgG) and salivary IgA. Despite a humoral immune response, all monkeys were infected after *H. pylori* challenge, and there were no differences in the density of colonization.

Immunization with urease therefore does not fully protect against challenge with *H. pylori*. An effective vaccine to prevent *H. pylori* infection will require different or more likely additional antigens, as well as improvements in the stimulation of the host immune response.

6/AB/7 (Item 7 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10641518 20187487 PMID: 10722611

Pilot study of phoP/phoQ-deleted *Salmonella enterica* serovar typhimurium expressing *Helicobacter pylori* urease in adult volunteers.

Angelakopoulos H; Hohmann E L

Infectious Disease Division, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts 02114; USA.

Infection and immunity (UNITED STATES) Apr 2000, 68 (4) p2135-41,  
ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: MO1 RR01066-21; RR; NCRR; RO1AI45137; AI; NIAID

Document type: Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Attenuated *Salmonella enterica* serovar Typhi has been studied as an oral vaccine vector. Despite success with attenuated *S. enterica* serovar Typhimurium vectors in animals, early clinical trials of *S. enterica* serovar Typhi expressing heterologous antigens have shown that few subjects have detectable immune responses to vectored antigens. A previous clinical study of phoP/phoQ-deleted *S. enterica* serovar Typhi expressing *Helicobacter pylori* urease from a multicopy plasmid showed that none of eight subjects had detectable immune responses to the vectored antigen. In an attempt to further define the variables important for engendering immune responses to vectored antigens in humans, six volunteers were inoculated with  $5 \times 10^7$  to  $8 \times 10^7$  CFU of phoP/phoQ-deleted *S. enterica* serovar Typhimurium expressing the same antigen. Two of the six volunteers had fever; none had diarrhea, bacteremia, or other serious side effects. The volunteers were more durably colonized than in previous studies of phoP/phoQ-deleted *S. enterica* serovar Typhi. Five of the six volunteers seroconverted to *S. enterica* serovar Typhimurium antigens and had strong evidence of anti-*Salmonella* mucosal immune responses by enzyme-linked immunospot studies. Three of six (three of five who seroconverted to *Salmonella*) had immune responses in the most sensitive assay of urease-specific immunoglobulin production by blood mononuclear cells in vitro. One of these had a fourfold or greater increase in end-point immunoglobulin titer in serum versus urease. Attenuated *S. enterica* serovar Typhimurium appears to be more effective than *S. enterica* serovar Typhi for engendering immune responses to urease. Data suggest that this may be related to a greater stability of antigen-expressing plasmid in *S. enterica* serovar Typhimurium and/or prolonged intestinal colonization. Specific factors unique to nontyphoidal salmonellae may also be important for stimulation of the gastrointestinal immune system.

6/AB/8 (Item 8 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10611753 20154333 PMID: 10689743

Accuracy of 13C-urea breath test in clinical use for diagnosis of *Helicobacter pylori* infection.

Riepl R L; Folwaczny C; Otto B; Klauser A; Blendinger C; Wiebecke B; Konig A; Lehnert P; Heldwein W

Medizinische Klinik, Klinikum Innenstadt, Ludwig-Maximilians-Universitat

Munchen, Germany.

Zeitschrift fur Gastroenterologie (GERMANY) Jan 2000, 38 (1) p13-9,  
ISSN 0044-2771 Journal Code: 0033370

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The 13C-urea breath test (UBT) is a noninvasive test for diagnosis of *Helicobacter pylori* infection of gastric mucosa. The aim of this prospective study was to assess the accuracy of a simple UBT in clinical routine use. METHODS: The study population comprised of 100 patients (49 f, 51 m) requiring diagnostic upper GI endoscopy. One biopsy specimen was taken from the gastric antrum, body and fundus, respectively, for standard histological examination and one additional specimen from each location was transformed into transport medium for cultivation of *H. pylori*. After vaccination of the culture plates the biopsies were tested for urease activity (UAT). After recovery from endoscopy the patients had to pass an one liter endexpiratory breath sample before and 15 min after drinking 200 ml orange juice, pH 3.6, containing 75 mg of 13C-urea. 13CO2 was measured in the breath samples using isotope-selective nondispersive infrared spectrometry. RESULTS: Defining gold standard groups with all biopsy tests (from antrum and corpus) positive or negative the 13CO2 delta over baseline (DOB) cut-off level of UBT was set at 6.5/1000 in order to best discriminate positive from negative patients (ROC analysis). UBT was positive in 37% of all subjects. Taken UAT and histological examination together (positive when both tests were positive) UBT displayed a sensitivity of 92%, a specificity of 94%, a positive predictive value of 89%, and a negative predictive value of 94%. When including the results of culture sensitivity and negative predictive value reached almost 100%. The mean of the 13CO2-DOB values from *H. pylori*-positive duodenal or gastric ulcer patients did not differ from controls (*H. pylori*-positive patients without lesions). The 13CO2-DOB values of the ulcer group were correlated significantly with the active inflammatory component of gastritis in antrum, corpus, and fundus. CONCLUSION: UBT with this setup detects *H. pylori* infection in clinical routine use with high accuracy. The increase of exhaled 13CO2 does not predict ulcer disease but reflects the degree of active inflammation of gastric mucosa.

6/AB/9 (Item 9 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

09243461 97118683 PMID: 8959525

Vaccination against *Helicobacter pylori*.

Lee A

School of Microbiology and Immunology, University of New South Wales,  
Sydney, Australia.

Journal of gastroenterology (JAPAN) Nov 1996, 31 Suppl 9 p69-74,  
ISSN 0944-1174 Journal Code: 9430794

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The initial steps have been taken towards the development of a vaccine against the human gastroduodenal pathogen, *Helicobacter pylori*. Proof of principle was achieved when mice were protected against challenge with living *Helicobacter felis*, a close relative of the human pathogen, following oral immunization with *H. felis* sonicate and the mucosal adjuvant, cholera toxin. Similar results with *H. pylori* antigen have allowed development of possible human vaccines. Recombinant urease protein has been proposed as a major vaccine candidate, together with

the heat-labile toxin of *Escherichia coli* as the adjuvant. Probably the most significant finding in the early vaccine studies was that immunization of already infected mice resulted in a cure of *Helicobacter* infection. The possibility of a therapeutic vaccine makes commercial development more attractive, as large populations could be immunized without the potential for development of drug-resistant strains that currently restricts widespread antibiotic use. For advanced societies with powerful economies yet a high prevalence of *H. pylori*, such as Japan, vaccine development should become a high national health priority.

6/AB/10 (Item 10 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

09238083 97142160 PMID: 8988394

Cell envelope characteristics of *Helicobacter pylori*: their role in adherence to mucosal surfaces and virulence.

Clyne M; Drumm B

Department of Paediatrics, University College Dublin, Our Ladys Hospital for Sick Children, Crumlin, Ireland.

FEMS immunology and medical microbiology (NETHERLANDS) Dec 1 1996, 16

(2) p141-55, ISSN 0928-8244 Journal Code: 9315554

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

*Helicobacter pylori* colonises the gastric mucosa of humans and causes both antral gastritis and duodenal ulcer disease. Exactly how *H. pylori* causes disease is not known but several pathogenic determinants have been proposed for the organism. These include adhesins, cytotoxins and a range of different enzymes including urease, catalase and superoxide dismutase. Surface molecules of *H. pylori* such as flagella, lipopolysaccharide, the urease enzyme and outer membrane proteins are putative adhesin molecules. While phosphatidylethanolamine and the Lewis(b) blood group antigen have been proposed as receptor molecules for the organism the exact mechanism by which *H. pylori* adheres to the gastric mucosa has still to be identified. Characterisation of the adhesins of *H. pylori* could lead to the development of adhesin analogues for use in the inhibition of colonisation and improved therapy for ulcer disease. In vivo studies with isogenic mutants which are incapable of adhering to the gastric mucosa would greatly clarify the significance of adherence. Such mutants could possibly be useful as a vaccine against infection with wild-type organisms.

6/AB/11 (Item 11 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

09181330 97067620 PMID: 8911016

*Helicobacter pylori* and gastroduodenal disorders: new approaches for prevention, diagnosis and treatment.

Kotloff K L

Department of Pediatrics, University of Maryland School of Medicine, Baltimore 21201, USA.

Vaccine (ENGLAND) Aug 1996, 14 (12) p1174-5, ISSN 0264-410X

Journal Code: 8406899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Prevention and treatment of *H. pylori* infection through immunization

would be an important achievement considering the high cost of drug therapy, the appearance of antibiotic resistant strains, and the failure of drug therapy to prevent reinfection. Success hinges on determining the extent to which immunologic memory can be evoked in the stomach, and the ability to identify antigens and delivery systems which stimulate protective immunity rather than disease-promoting responses. Recent experiments by several groups have demonstrated that mice immunized orally or intragastrically (along with mucosal adjuvant) with whole *H. pylori* lysate, purified or recombinant urease, or purified VacA were significantly protected against challenge with virulent *Helicobacter*. Several vaccine candidates will enter clinical trials in humans in the near future.

6/AB/12 (Item 12 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

08802740 96153005 PMID: 8563056  
Animal models and vaccine development.

Lee A  
School of Microbiology and Immunology, University of New South Wales,  
Kensington, Sydney, Australia.

Bailliere's clinical gastroenterology (ENGLAND) Sep 1995, 9 (3)  
p615-32, ISSN 0950-3528 Journal Code: 8704786

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Following the demonstration of *Helicobacter pylori* as a major gastroduodenal pathogen there was a need to develop animal models in order to investigate mechanisms of pathogenesis and to be able to test new treatment strategies. *Helicobacter pylori* will only colonize a limited number of hosts including non-human primates, germ-free or barrier raised piglets, germ-free dogs and recently laboratory raised cats. Although these models have proved useful there is a need for more convenient small animal models. The ferret infected with its natural gastric organism, *Helicobacter mustelae*, is the only other animal to show peptic ulceration and has been successfully used to investigate gastritis and antimicrobial agents. The other commonly used animal model is the laboratory mouse or rat infected with either *Helicobacter felis* or *Helicobacter heilmannii*, bacteria that normally colonize cat or dog gastric mucosae. Active/chronic gastritis, gastric atrophy, and lymphoma-like lesions have been shown to develop in *H. felis* infected mice. The most recent and exciting use of an animal model has been the use of the *H. felis* mouse model in the development of human vaccines against *H. pylori*. Mice can be protected against infection with large doses of viable *H. felis* by oral immunization using sonicates of *H. felis* or *H. pylori* or recombinant *H. pylori* urease together with cholera toxin or cholera toxin-B subunit as the mucosal adjuvant. More importantly it has been shown that immunization of already infected animals results in eradication of infection. This raises the intriguing possibility that therapeutic immunization might be a viable option in the management of *Helicobacter*-associated disease. If immunization as a therapy of peptic ulcers was combined with short-term acid suppression, the possibility of reinfection may also be eliminated. In those countries where *H. pylori* infection rates are very high and infection occurs at an early age, large scale oral immunization of sections of the community would not only protect the young from the deleterious consequences of long-term *H. pylori* infection but could also cure existing disease.

6/AB/13 (Item 13 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

08761383 96100076 PMID: 8574728  
Vaccine strategies for prevention of *Helicobacter pylori* infection.  
Sellman S; Blanchard T G; Nedrud J G; Czinn S J  
Department of Pediatrics, Case Western Reserve University, Cleveland,  
Ohio, USA.  
European journal of gastroenterology & hepatology (ENGLAND) Aug 1995,  
7 Suppl 1 pS1-6, ISSN 0954-691X Journal Code: 9000874  
Contract/Grant No.: DK 46461; DK; NIDDK; HL-37117; HL; NHLBI  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed

OBJECTIVE: To examine the level and duration of the humoral immune response to *Helicobacter felis* following oral immunization or infection.  
DESIGN AND METHODS: Germ-free mice were orally immunized with sonicated *H . felis* plus cholera toxin five times over 6 weeks. One week after immunization was completed, immunized and control non-immunized mice received an oral challenge of live *H . felis* organisms. The animals were killed at 3-week intervals and serum, gastric washings, intestinal washings and gastric biopsies were obtained. *H . felis* infection was confirmed by a positive urease test or culture of the gastric biopsy. Serum gastric and intestinal antibody titers were determined by enzyme-linked immunosorbent assay. CONCLUSION: Infection and immunization against *H . felis* produces a specific humoral response. The humoral response in infection alone is significantly smaller than that of immunized animals until 6 weeks after infection. The humoral response following oral immunization persists for at least 18 weeks without further stimulation. The presence of an *H . felis*-specific antibody immune response before infection may be needed to protect animals from acute *Helicobacter* infection.

6/AB/14 (Item 14 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

08569258 95327674 PMID: 7604021  
The GroES homolog of *Helicobacter pylori* confers protective immunity against mucosal infection in mice.  
Ferrero R L; Thiberge J M; Kansau I; Wuscher N; Huerre M; Labigne A  
Unite des Enterobacteries, Institut National de la Sante et de la Recherche Medicle U389, Paris, France.  
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jul 3 1995, 92 (14) p6499-503, ISSN 0027-8424  
Journal Code: 7505876  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed

*Helicobacter pylori* is an important etiologic agent of gastroduodenal disease. In common with other organisms, *H . pylori* bacteria express heat shock proteins that share homologies with the GroES-GroEL class of proteins from *Escherichia coli*. We have assessed the heat shock proteins of *H . pylori* as potential protective antigens in a murine model of gastric *Helicobacter* infection. Orogastric immunization of mice with recombinant *H . pylori* GroES- and GroEL-like proteins protected 80% (n = 20) and 70% (n = 10) of animals, respectively, from a challenge dose of 10(4) *Helicobacter felis* bacteria (compared to control mice, P = 0.0042 and P = 0.0904, respectively). All mice (n = 19) that were immunized with a dual



antigen preparation, consisting of *H. pylori* GroES-like protein and the B subunit of *H. pylori* urease, were protected against infection. This represented a level of protection equivalent to that provided by a sonicated *Helicobacter* extract ( $P = 0.955$ ). Antibodies directed against the recombinant *H. pylori* antigens were predominantly of the IgG1 class, suggesting that a type 2 T-helper cell response was involved in protection. This work reports a protein belonging to the GroES class of heat shock proteins that was shown to induce protective immunity. In conclusion, GroES-like and urease B-subunit proteins have been identified as potential components of a future *H. pylori* subunit vaccine.

6/AB/15 (Item 15 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

08561272 95318517 PMID: 7797906

Oral immunization with recombinant *Helicobacter pylori* urease induces secretory IgA antibodies and protects mice from challenge with *Helicobacter felis*.

Lee C K; Weltzin R; Thomas W D; Kleanthous H; Ermak T H; Soman G; Hill J E; Ackerman S K; Monath T P

OraVax, Inc., Cambridge, MA 02139, USA.

Journal of infectious diseases (UNITED STATES) Jul 1995, 172 (1)  
p161-72, ISSN 0022-1899 Journal Code: 0413675

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

*Helicobacter pylori*, a gram-negative spiral bacterium, is the cause of chronic superficial (type B) gastritis and peptic ulcer disease. The urease enzyme of *H. pylori* was expressed as an inactive recombinant protein in *Escherichia coli*, purified as particulate structures of 550-600 kDa molecular mass with a diameter of approximately 12 nm. Given orally, 5 micrograms of urease with an appropriate mucosal adjuvant, such as the labile toxin of *E. coli*, protected 60%-100% of mice against challenge with virulent *Helicobacter felis*. Protection correlated with the level of secretory IgA antibodies against urease. Oral administration of antigen was as effective or better than intragastric administration. Parenteral injection of antigen or intragastric administration of high-dose antigen without adjuvant elicited serum IgG but no IgA antibodies and did not confer protection. Recombinant urease as an oral vaccine candidate deserves further investigation as an approach to the prevention of *Helicobacter*-induced chronic gastroduodenal diseases in humans.

6/AB/16 (Item 16 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

08560401 95317528 PMID: 7797009

Oral immunization with *Helicobacter pylori* urease B subunit as a treatment against *Helicobacter* infection in mice.

Corthesy-Theulaz I; Porta N; Glauser M; Saraga E; Vaney A C; Haas R; Kraehenbuhl J P; Blum A L; Michetti P

Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.

Gastroenterology (UNITED STATES) Jul 1995, 109 (1) p115-21, ISSN 0016-5085 Journal Code: 0374630

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND & AIMS: Eradication of *Helicobacter pylori* infections in humans results in the healing of gastritis and gastric ulcers. This study used a mouse model to test whether oral vaccination can cure *Helicobacter* infection and gastritis. METHODS: Mice were infected with *Helicobacter felis*. Three weeks after infection, the mice were orally immunized with *H. pylori* urease B subunit. Control mice were simultaneously infected but sham immunized. RESULTS: Three to 8 weeks after oral immunization of *H. felis*-infected mice with recombinant *H. pylori* urease B subunit, the infection cleared and there was no evidence of gastritis. Vaccinated mice remained protected against two consecutive *H. felis* challenges. CONCLUSIONS: These results show that the lack of natural immunity against *Helicobacter* can be overcome by oral immunization and that vaccination offers a novel therapeutic approach to *Helicobacter*-induced gastritis.

6/AB/17 (Item 17 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)

08448748 95197244 PMID: 7890380  
Effect of oral immunization with recombinant urease on murine *Helicobacter felis* gastritis.  
Pappo J; Thomas W D; Kabok Z; Taylor N S; Murphy J C; Fox J G  
Vaccine Delivery Research Section, OraVax Inc., Cambridge, Massachusetts  
02139.

Infection and immunity (UNITED STATES) Apr 1995, 63 (4) p1246-52,  
ISSN 0019-9567 Journal Code: 0246127  
Contract/Grant No.: 5-P01-CA26731; CA; NCI; AI34679; AI; NIAID; DK 36563;  
DK; NIDDK; +

Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed

The ability of oral immunization to interfere with the establishment of infection with *Helicobacter felis* was examined. Groups of Swiss Webster mice were immunized orally with 250 micrograms of *Helicobacter pylori* recombinant urease (rUrease) and 10 micrograms of cholera toxin (CT) adjuvant, 1 mg of *H. felis* sonicate antigens and CT, or phosphate-buffered saline (PBS) and CT. Oral immunization with rUrease resulted in markedly elevated serum immunoglobulin G (IgG), serum IgA, and intestinal IgA antibody responses. Challenge with live *H. felis* further stimulated the urease-specific intestinal IgA and serum IgG and IgA antibody levels in mice previously immunized with rUrease but activated primarily the serum IgG compartment of PBS-treated and *H. felis*-immunized mice. Intestinal IgA and serum IgG and IgA anti-urease antibody responses were highest in rUrease-immunized mice at the termination of the experiment. Mice immunized with rUrease were significantly protected ( $P < \text{or} = 0.0476$ ) against infection when challenged with *H. felis* 2 or 6 weeks post-oral immunization in comparison with PBS-treated mice. Whereas *H. felis*-infected mice displayed multifocal gastric mucosal lymphoid follicles consisting of CD45R+ B cells surrounded by clusters of Thyl.2+ T cells, gastric tissue from rUrease-immunized mice contained few CD45R+ B cells and infrequent mucosal follicles. These observations show that oral immunization with rUrease confers protection against *H. felis* infection and suggest that gastric tissue may function as an effector organ of the mucosal immune system which reflects the extent of local antigenic stimulation.

6/AB/18 (Item 18 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)

08254207 95011230 PMID: 7926454

Immunization of BALB/c mice against *Helicobacter felis* infection with *Helicobacter pylori* urease.

Michetti P; Cortesy-Theulaz I; Davin C; Haas R; Vaney A C; Heitz M; Bille J; Kraehenbuhl J P; Saraga E; Blum A L

Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.

Gastroenterology (UNITED STATES) Oct 1994, 107 (4) p1002-11, ISSN 0016-5085 Journal Code: 0374630

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND/AIMS: Because *Helicobacter pylori* is a potentially dangerous human pathogen, the protective potential of oral immunization with *H. pylori* urease and its subunits was evaluated in an animal model. METHODS: Mice were orally immunized with *H. pylori* sonicate, urease, or recombinant enzymatically inactive urease subunits and then challenged with *Helicobacter felis*. Control mice were sham-immunized. RESULTS: *H. felis* colonization was present 5 days after challenge in 9 of 10 sham-immunized, 6 of 9 sonicate-immunized, and 3 of 10 urease-immunized animals ( $P = 0.031$  vs. sham-immunized). Twelve days after challenge, urease B-immunized mice had a weaker colonization than sham-immunized controls, whereas urease A had no effect. After 70 days, most urease A- and urease B-immunized mice had cleared the colonization (10/17:  $P = 0.0019$ ; 16/20:  $P = 0.00002$  vs. sham-immunized). In urease B-immunized animals, protection was often associated with corpus gastritis. CONCLUSIONS: Oral immunization with *H. pylori* urease protects mice against *H. felis* infection. Enzymatically inactive urease A and B subunits contain protective epitopes. It is unclear whether protection depends on the development of a mononuclear inflammatory response in the gastric corpus. Our observations should encourage the development of a human vaccine.

6/AB/19 (Item 19 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

08121494 94237422 PMID: 8181696

Lack of protection against gastric *Helicobacter* infection following immunisation with jack bean urease: the rejection of a novel hypothesis.

Chen M; Lee A; Hazell S L; Hu P; Li Y

School of Microbiology and Immunology, University of New South Wales, Kensington, Australia.

FEMS microbiology letters (NETHERLANDS) Mar 1 1994, 116 (3) p245-50, ISSN 0378-1097 Journal Code: 7705721

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The common mucosal immune system was stimulated by oral immunisation with jack bean urease and the adjuvant cholera toxin. A high level of local antibody and serum antibody was induced in mice following hyperimmunisation with this combination. No cross-reacting antibody was found against either *Helicobacter pylori* or *Helicobacter felis*. No protection was observed against oral challenge of immunised mice with living *H. felis* thus disproving the interesting hypothesis of Pallen and Clayton that plant urease might induce a protective immunity against *helicobacter* infection.

6/AB/20 (Item 20 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)

08029016 94156469 PMID: 8112850

Immunological and molecular characterization of *Helicobacter felis* urease.

Gootz T D; Perez-Perez G I; Clancy J; Martin B A; Tait-Kamradt A; Blaser M J

Department of Immunology and Infectious Diseases, Central Research Division, Pfizer Inc., Groton, Connecticut 06340.

Infection and immunity (UNITED STATES) Mar 1994, 62 (3) p793-8,  
ISSN 0019-9567 Journal Code: 0246127

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Urease activity has recently been shown to be an important virulence determinant for *Helicobacter pylori*, allowing it to survive the low pH of the stomach during colonization. Experimental murine infection with *Helicobacter felis* is now being used as a model for *H. pylori* infection to study the effects of vaccines, antibiotics, and urease inhibitors on colonization. However, little information comparing the ureases of *H. felis* and *H. pylori* is available. Urease was partially purified from the cell surface of *H. felis* ATCC 49179 by A-5M agarose chromatography, resulting in an eightfold increase in specific activity over that of crude urease. The apparent  $K_m$  for urea for the partially purified urease was 0.4 mM, and the enzyme was inhibited in a competitive manner by fluoroamide (50% inhibitory concentration = 0.12 micromM). Antiserum to whole cells of

*H. pylori* recognized both *H. pylori* and *H. felis* urease B subunits. Antiserum raised against *H. felis* whole cells recognized the large and small autologous urease subunits and the cpn60 heat shock molecule in both *H. felis* and *H. pylori*. However, this antiserum showed only a weak reaction with the B subunit of *H. pylori* urease. Two oligomeric DNA sequences were used as probes to evaluate the relatedness of *H. felis* and *H. pylori* urease gene sequences. One 30-mer from the ureA sequence, which had been shown previously to be specific for *H. pylori*, failed to hybridize to *H. felis* genomic DNA. A probe to the putative coding sequence for the active site of the *H. pylori* ureB subunit hybridized at low intensity to a 2.8-kb fragment of BamHI-HindIII-digested *H. felis* DNA, suggesting that the sequences were homologous but not identical, a result confirmed from the recently published sequences of ureA and ureB from *H. felis*.

6/AB/21 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12900306 BIOSIS NO.: 200100107455

Evaluation of factors that can affect protective immune responses following oral immunization of recombinant *Helicobacter pylori* urease apoenzyme.

AUTHOR: Kim Jang Seong; Chang Ji Hoon; Park Eun Jeong; Chung Soo Il; Yum Jung Sun(a)

AUTHOR ADDRESS: (a)Mogam Biotechnology Research Institute, 341 Pojung-Ri, Koosung-Myon, Yongin, Kyonggi-Do, 449-910: jsyum@greencross.com\*\*South Korea

JOURNAL: Journal of Microbiology and Biotechnology 10 (6):p865-872  
December, 2000

MEDIUM: print

ISSN: 1017-7825

DOCUMENT TYPE: Article

RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

ABSTRACT: *Helicobacter pylori* is the major cause of gastritis, peptic ulcer, and a principal risk factor for gastric cancer. As the first step towards a vaccine against *H. pylori* infection, *H. pylori* urease was expressed and purified as a recombinant apoenzyme (rUrease) in *E. coli*. In order to develop an effective immunization protocol using rUrease, the host immune responses were evaluated after the oral immunization of mice with rUrease preparations plus cholera toxin relative to various conditions, such as the physical nature of the antigen, the frequency of the booster immunization, the dose of the antigen, and the route of administration. The protective efficacy was assessed using a quantitative culture following an *H. pylori* SS1 challenge. It was demonstrated that rUrease, due to its particulate nature, was more superior than the UreB subunit as a vaccine antigen. The oral immunization of rUrease elicited significant systemic and secretory antibody responses, and activated predominantly Th2-type cellular responses. The bacterial colonization was significantly reduced (approx 100-fold) in those mice immunized with three or four weekly oral doses of rUrease plus cholera toxin ( $p < 0.05$ ), when compared to the non-immunized/challenged controls. The protection correlated well with the elicited secretory IgA level against rUrease, and these secretory antibody responses were highly dependent on the frequency of the booster immunization, yet unaffected by the dose of the antigen (25-200  $\mu$ g). These results demonstrate the remarkable potential of rUrease as a vaccine antigen, thereby strengthening the possibility of developing an *H. pylori* vaccine for humans.

2000

6/AB/22 (Item 2 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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10769777 BIOSIS NO.: 199799390922  
Resolution of gastritis and duration of protection against *H. felis* infection after oral immunization with recombinant urease.  
AUTHOR: Ermak T H; Kleanthous H K; Myers G; Ding R; Lee C K; Pappo J; Monath T P  
AUTHOR ADDRESS: OraVax Inc., Cambridge, MA\*\*USA  
JOURNAL: Gut 39 (SUPPL. 2):pA45 1996  
CONFERENCE/MEETING: IXth International Workshop on Gastroduodenal Pathology and *Helicobacter pylori* Copenhagen, Denmark October 16-19, 1996  
ISSN: 0017-5749  
RECORD TYPE: Citation  
LANGUAGE: English  
1996

6/AB/23 (Item 3 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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10699777 BIOSIS NO.: 199799320922  
Immunomagnetic bead enrichment and PCR for detection of *Helicobacter pylori* in human stools.  
AUTHOR: Nilsson Hans-Olof; Almljun Par(a); Nilsson Ingrid; Tyszkiewicz Tadeusz; Wadstrom Torkel  
AUTHOR ADDRESS: (a) Dep. Med. Microbiol., Univ. Lund, Solvegatan 23, S-223

62 Lund\*\*Sweden  
 JOURNAL: Journal of Microbiological Methods 27 (1):p73-79 1996  
 ISSN: 0167-7012  
 RECORD TYPE: Abstract  
 LANGUAGE: English

ABSTRACT: An immunomagnetic bead-based polymerase chain reaction assay (IMS-PCR) was developed for the detection of *Helicobacter pylori* in experimentally inoculated human stools and human clinical stool samples. Magnetic beads coated with anti- *H. pylori* rabbit antibodies were used for enrichment and concentration of *H. pylori* from faecal samples. Taq polymerase inhibitors, found in human faeces, are efficiently removed by the immunomagnetic separation (IMS) and subsequent washing of the magnetic beads. Conditions of the assay were developed and optimised with faeces from a healthy, *H. pylori* seronegative, individual. Faeces was inoculated with serial dilutions of either the spiral or the coccoid form of *H. pylori*. These two morphologic forms could be detected at similar concentrations when inoculated in faeces using an optimised IMS-PCR method. In 1 g of faeces less than 2.5 times  $10^{-4}$  *H. pylori* cells were detected as measured with two separate sets of PCR-primers, based on a urease A subunit gene sequence and a gene sequence encoding a 26 kDa surface protein of *H. pylori*. Previously no report has shown a sensitivity below  $10^{-6}$  *H. pylori* in faeces PCR. Preliminary analysis of stool samples from 17 patients with symptoms of gastritis and esophagitis by IMS-PCR showed a good correlation with EIA-analysis of *H. pylori* serum-antibodies from these patients. The results indicate that *H. pylori* cells are shed in faeces of infected patients and that immunomagnetic bead PCR might be an appropriate method for clinical diagnosis and studies involving immunoprophylaxis, antibiotic treatment as well as vaccine candidates.

1996

6/AB/24 (Item 4 from file: 5)  
 DIALOG(R)File 5: BIOSIS Previews(R)  
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10398311 BIOSIS NO.: 199699019456  
 Oral vaccination with recombinant urease reduces gastric  
*Helicobacter pylori* colonization in the cat.  
 AUTHOR: Batchelder M(a); Fox J G(a); Monath T; Yan L(a); Attardo L;  
 Georgakopoulos K; Li X(a); Marini R(a); Shen Z(a); Pappo J; Lee C  
 AUTHOR ADDRESS: (a)Div. Comparative Med., Massachusetts Inst. Technol.,  
 Cambridge, MA\*\*USA  
 JOURNAL: Gastroenterology 110 (4 SUPPL.):pA58 1996  
 CONFERENCE/MEETING: 96th Annual Meeting of the American Gastroenterological  
 Association and the Digestive Disease Week San Francisco, California, USA  
 May 19-22, 1996  
 ISSN: 0016-5085  
 RECORD TYPE: Citation  
 LANGUAGE: English  
 1996

6/AB/25 (Item 5 from file: 5)  
 DIALOG(R)File 5: BIOSIS Previews(R)  
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09827770 BIOSIS NO.: 199598282688  
*Helicobacter pylori* and cancer prone lesions of the stomach.

AUTHOR: De Koster E; Buset M; Fernandes E; Deltenre M  
 AUTHOR ADDRESS: Brugmann Univ. Hosp.\*\*Belgium  
 JOURNAL: Acta Endoscopica 25 (1):p33-44 1995  
 ISSN: 0240-642X  
 DOCUMENT TYPE: Literature Review  
 RECORD TYPE: Abstract  
 LANGUAGE: French; Non-English  
 SUMMARY LANGUAGE: French; English

ABSTRACT: Gastric cancer still is a major health problem, in spite of its declining incidence. Its histopathogenesis is described in the Correa model, where environmental influences cause the evolution from a normal stomach through superficial and atrophic gastritis to intestinal metaplasia, dysplasia, and finally carcinoma. *Helicobacter pylori* is the main causative agent of chronic active gastritis. As chronic atrophic gastritis progresses, the density of the bacteria diminishes, and in severe atrophic gastritis, only serum antibodies against *H. pylori* remain. The development of chronic atrophic gastritis is associated with the presence of *H. pylori*, high gastric juice pH, low gastric juice vitamin C, and low serum levels of beta-carotene. Intestinal metaplasia is likewise associated with *H. pylori* low intake and gastric juice levels of vitamin C, high gastric juice pH, and bile reflux. High rates of *H. pylori* prevalence can also be found in patients with dysplasia and early gastric cancer; the role of *H. pylori* in the diffuse type of early gastric cancer is debated. Mechanisms involved in carcinogenesis include *H. pylori*-induced inflammation, with increased gastric cell proliferation and mutagenic inflammatory products; *H. pylori*-enabled stimulation of gastric cell proliferation by salt; *H. pylori*-induced abolishment of the gastric vitamin C concentration mechanism; *H. pylori* urease-produced ammonia, which is able in itself to induce atrophy; and *H. pylori* toxin, which is important in gastric carcinogenesis for unknown reasons. It is unknown whether some of the precancerous lesions are reversible or preventable; *H. pylori* eradication in selected patients and population-based vaccination should be evaluated.

1995

6/AB/26 (Item 6 from file: 5)  
 DIALOG(R)File 5:Biosis Previews(R)  
 (c) 2002 BIOSIS. All rts. reserv.

09551987 BIOSIS NO.: 199598006905  
 Recombinant Antigens Prepared from the Urease Subunits of *Helicobacter* spp.: Evidence of Protection in a Mouse Model of Gastric Infection.  
 AUTHOR: Ferrero Richard L(a); Thiberge Jean-Michel; Huerre Michel; Labigne Agnes  
 AUTHOR ADDRESS: (a)Unite Enterobacteries, Inst. Pasteur, 28 du Rue Dr. Roux, Paris 75724\*\*France  
 JOURNAL: Infection and Immunity 62 (11):p4981-4989 1994  
 ISSN: 0019-9567  
 DOCUMENT TYPE: Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English

ABSTRACT: Urease is an important virulence factor for gastric *Helicobacter* spp. To elucidate the efficacy of individual urease subunits to act as mucosal immunogens, the genes encoding the respective urease subunits (UreA and UreB) of *Helicobacter pylori* and *Helicobacter felis* were cloned in an expression vector (pMAL) and

expressed in *Escherichia coli* cells as translational fusion proteins. The recombinant UreA and UreB proteins were purified by affinity and anion-exchange chromatography techniques and had predicted molecular masses of approximately 68 and 103 kDa, respectively. Western blotting (immunoblotting) studies indicated that the urease components of the fusion proteins were strongly immunogenic and were specifically recognized by polyclonal rabbit anti-*Helicobacter* sp. sera. The fusion proteins (50 µg) were used, in combination with a mucosal adjuvant (cholera toxin), to orogastrically immunize mice against *H. felis* infection. Gastric tissues from *H. felis*-challenged mice were assessed by the biopsy urease test and by histology. In mice immunized with recombinant *H. felis* UreB, 60% of animals (n = 7) were histologically negative for *H. felis* bacteria after challenge at 17 weeks. This compared with 25% (n = 8) for mice immunized with the heterologous *H. pylori* UreB antigen. Neither the homologous nor the heterologous UreA subunit elicited protective responses against *H. felis* infection in mice. The study demonstrated that a recombinant subunit antigen could induce an immunoprotective response against gastric *Helicobacter* infection.

1994

6/AB/27 (Item 1 from file: 34)  
 DIALOG(R) File 34:SciSearch(R) Cited Ref Sci  
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08686654 Genuine Article#: 317AT Number of References: 37  
 Title: Accuracy of C-13-urea breath test in clinical use for diagnosis of *Helicobacter pylori* infection (ABSTRACT AVAILABLE)  
 Author(s): Riepl RL (REPRINT) ; Folwaczny C; Otto B; Klauser A; Blendinger C; Wiebecke B; Konig A; Lehnert P; Heldwein W  
 Corporate Source: UNIV MUNICH, MED KLIN, KLINIKUM INNENSTADT, ZIEMSENSTR 1/D-80336 MUNICH//GERMANY/ (REPRINT); UNIV MUNICH, INST PATHOL, KLINIKUM INNENSTADT/D-80336 MUNICH//GERMANY/; MAX VON PETTENKOFER INST, /D-8000 MUNICH//GERMANY/  
 Journal: ZEITSCHRIFT FUR GASTROENTEROLOGIE, 2000, V38, N1 (JAN), P13-19  
 ISSN: 0044-2771 Publication date: 20000100  
 Publisher: DEMETER VERLAG GEORG THIEME VERLAG, PETRA SCHLAGENHAUF, RUDIGERSTR 14, D-70469 STUTTGART, GERMANY  
 Language: English Document Type: ARTICLE  
 Abstract: The C-13-urea breath test (UBT) is a noninvasive test for diagnosis of *Helicobacter pylori* infection of gastric mucosa. The aim of this prospective study was to assess the accuracy of a simple UBT in clinical routine use.

Methods: The study population comprised of 100 patients (49 f, 51 m) requiring diagnostic upper CT endoscopy. One biopsy specimen was taken from the gastric antrum, body and fundus, respectively, for standard histological examination and one additional, specimen from each location was transformed into transport medium for cultivation of *H. pylori*. After vaccination of the culture plates the biopsies were tested for urease activity (UAT). After recovery from endoscopy the patients had to pass an one liter endexpiratory breath sample before and 15 min after drinking 200 ml orange juice, pH 3.6, containing 75 mg of C-13-urea. (CO<sub>2</sub>)-C-13 was measured in the breath samples using isotope-selective nondispersive infrared spectrometry.

Results: Defining gold standard groups with all biopsy tests (from antrum and corpus) positive or negative the (CO<sub>2</sub>)-C-13 delta over baseline (DOB) cut-off level of UBT was set at 6.5 parts per thousand



in order to best discriminate positive from negative patients (ROC analysis). UBT was positive in 37% of all subjects. Taken UAT and histological examination together (positive when both tests were positive) UBT displayed a sensitivity of 92%, a specificity of 94%, a positive predictive value of 89%, and a negative predictive value of 94%. When including the results of culture sensitivity and negative predictive value reached almost 100%. The mean of the (CO<sub>2</sub>)-C-13-DOB values from *H. pylori*-positive duodenal or gastric ulcer patients did not differ from controls (*H. pylori*-positive patients without lesions). The (CO<sub>2</sub>)-C-13-DOB values of the ulcer group were correlated significantly with the active inflammatory component of gastritis in antrum, corpus, and fundus.

Conclusion: UBT with this setup detects *H. pylori* infection in clinical routine use with high accuracy. The increase of exhaled (CO<sub>2</sub>)-C-13 does not predict ulcer disease but reflects the degree of active inflammation of gastric mucosa.

6/AB/28 (Item 2 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

08480768 Genuine Article#: 290JW Number of References: 23  
Title: Development of a new method for the determination of immune responses in the human stomach (ABSTRACT AVAILABLE)  
Author(s): Bergquist C; MattssonRydberg A; Lonroth H; Svennerholm AM (REPRINT)  
Corporate Source: GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL, GULDHEDSGATAN 10A/S-41346 GOTHENBURG//SWEDEN/ (REPRINT); GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL/S-41346 GOTHENBURG//SWEDEN/; GOTHENBURG UNIV, DEPT SURG/S-41346 GOTHENBURG//SWEDEN/  
Journal: JOURNAL OF IMMUNOLOGICAL METHODS, 2000, V234, N1-2 (FEB 3), P51-59  
ISSN: 0022-1759 Publication date: 20000203  
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS  
Language: English Document Type: ARTICLE  
Abstract: The discovery of the gastric pathogen *Helicobacter pylori* has created a need for accurate methods to study immune responses locally in the human stomach. Therefore, we have developed a quick and easy method for extraction of antibodies from gastric biopsies using saponin and compared this method with the more laborious analysis of antibody-secreting cells (ASCs) from gastric biopsies. We have also analyzed the antibody content in gastric aspirates, saliva and plasma. There was a strong correlation between the total IgA levels in the biopsy extracts and the frequencies of IgA-secreting cells. In addition, the IgA and IgG levels against a *H. pylori* whole membrane preparation and purified urease in the biopsy extracts correlated well with the frequencies of specific IgA and IgG secreting cells. However, the antibody levels in gastric aspirates, saliva and plasma specimens did not correlate with the frequencies of corresponding ASC in the gastric biopsies. Thus, the saponin extraction method is suitable for monitoring local antibody responses in the stomach, while analyses of gastric aspirates, saliva or plasma are not appropriate for this purpose. (C) 2000 Elsevier Science B.V. All rights reserved.

6/AB/29 (Item 3 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

08296686 Genuine Article#: 268KH Number of References: 97  
Title: Pathogenesis of Helicobacter pylori infection (ABSTRACT AVAILABLE)  
Author(s): McGee DJ; Mobley HLT (REPRINT)  
Corporate Source: UNIV MARYLAND, SCH MED, DEPT MICROBIOL & IMMUNOL, 655 W  
BALTIMORE ST/BALTIMORE//MD/21201 (REPRINT); UNIV MARYLAND, SCH MED, DEPT  
MICROBIOL & IMMUNOL/BALTIMORE//MD/21201  
Journal: CURRENT OPINION IN GASTROENTEROLOGY, 2000, V16, N1 (JAN), P24-31  
ISSN: 0267-1379 Publication date: 20000100  
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA  
19106-3621

Language: English Document Type: ARTICLE

Abstract: Helicobacter pylori, a gram-negative, microaerophilic, motile, spiral-shaped bacterium, has been established as the etiologic agent of gastritis and peptic ulcers and is a major risk factor for gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma (MALT). The ability of H. pylori to cause this spectrum of diseases depends on host, bacterial, and environmental factors. Bacterial factors critical for H. pylori colonization of the gastric mucosa include urease, flagella, adhesins, and delta-glutamyltranspeptidase. Lipopolysaccharide, urease, and vacuolating cytotoxin are among the factors that allow H. pylori to persist for decades and invoke an intense inflammatory response, leading to damaged host cells. Genes in the cag pathogenicity island also contribute to the inflammatory response by initiating a signal transduction cascade, resulting in interleukin-8 production. Proinflammatory cytokines and a Th-1 cytokine response further exacerbates the inflammation. Products of the enzymes nitric oxide synthase (iNOS) and cyclooxygenase may perturb the balance between gastric epithelial cell apoptosis (ulcer formation) and proliferation (cancer). The host Th-1 response and antibodies directed against H. pylori do not eliminate the organism, which presents challenges to vaccine development. Vaccines that include urease have shown some promise, but improved adjuvants and animal models should hasten progress in vaccine research. H. pylori is the most genetically diverse organism known, and the panmictic population structure may contribute to the varying ranges of disease severity produced by different strains. The complete genome sequence of two strains of H. pylori has propelled this field forward, and numerous groups are now using genomic, proteomic, and mutagenetic approaches to identify new virulence genes. Discovered only in 1982, H. pylori is now among the most intensely investigated organisms. This review summarizes recent progress in this rapidly moving field. (C) 2000 Lippincott Williams & Wilkins, Inc.

6/AB/30 (Item 4 from file: 34)  
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

05464486 Genuine Article#: WA686 Number of References: 93  
Title: HELICOBACTER-PYLORI - CAN THE MECHANISMS OF PATHOGENESIS GUIDE US  
TOWARDS NOVEL STRATEGIES FOR TREATMENT AND PREVENTION (Abstract  
Available)  
Author(s): FALK P  
Corporate Source: KAROLINSKA INST, DEPT MED, GASTROINTESTINAL RES LAB/S-17176  
STOCKHOLM//SWEDEN//; WASHINGTON UNIV, SCH MED, DEPT MOL BIOL &  
PHARMACOL/ST LOUIS//MO/63110  
Journal: JOURNAL OF INTERNAL MEDICINE, 1996, V240, N6 (DEC), P319-332  
ISSN: 0954-6820  
Language: ENGLISH Document Type: REVIEW  
Abstract: Helicobacter pylori establishes a chronic infection in the  
stomach of humans. The infection is associated with a low grade

inflammatory response in the epithelium that can develop into chronic active gastritis , peptic ulcer disease or neoplasia. Antibiotics have dramatically decreased the rate of recurrence of peptic ulcers . However, antibiotic resistance is already evident, casting doubts on the future efficacy of these strategies. The link between childhood infection and severe health problems, including increased risk for gastric tumours motivate efforts to develop vaccines . Characterization of the molecular mechanisms of pathogenesis will pave the way for novel strategies for treatment and prevention of H. pylori infection.

6/AB/31 (Item 5 from file: 34)  
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
 (c) 2002 Inst for Sci Info. All rts. reserv.

05420678 Genuine Article#: VX237 Number of References: 43  
 Title: STRATEGIES FOR AN ORAL VACCINE AGAINST HELICOBACTER-PYLORI (Abstract Available)  
 Author(s): FERRERO RL; LABIGNE A  
 Corporate Source: INST PASTEUR,UNITE PATHOGENIE BACTERIENNE MUQUEUSES  
 INSERM U38,28 RUE DR ROUX/F-75724 PARIS//FRANCE/  
 Journal: CURRENT OPINION IN GASTROENTEROLOGY, 1996, V12, N6 (NOV), P564-568  
 ISSN: 0267-1379  
 Language: ENGLISH Document Type: ARTICLE  
 Abstract: Helicobacter pylori is an etiologic agent of chronic gastritis , peptic ulcer disease, and gastric carcinogenesis in humans. Infection with H . pylori is common, with prevalence rates varying between 20% and 90%, depending on the population surveyed. Vigorous immune responses to H . pylori are observed in infected individuals, yet these responses are generally inadequate in eradicating the bacterium. Experiments in various animal models have established that immunization via the orogastric route can induce protective mucosal immune responses against gastric Helicobacter infections. Moreover, it was shown that active immunization could be used to eradicate an existent infection. Recently, several defined Helicobacter antigens were validated to be effective mucosal immunogens. One of these antigens ( urease ) has reached the clinical trial phase, Research toward the development of an H . pylori subunit vaccine has revealed that the stomach is a bona fide component of the common mucosal immune system.

6/AB/32 (Item 6 from file: 34)  
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
 (c) 2002 Inst for Sci Info. All rts. reserv.

05309200 Genuine Article#: VP428 Number of References: 46  
 Title: EFFECT OF GROWTH-PHASE AND ACID SHOCK ON HELICOBACTER-PYLORI CAGA EXPRESSION (Abstract Available)  
 Author(s): KARITA M; TUMMURU MKR; WIRTH HP; BLASER MJ  
 Corporate Source: VANDERBILT UNIV,SCH MED,DEPT MED,DIV INFECT DIS,A-3310  
 MED CTR N/NASHVILLE//TN/37232; VANDERBILT UNIV,SCH MED,DEPT MED,DIV  
 INFECT DIS/NASHVILLE//TN/37232; DEPT VET AFFAIRS MED CTR,INFECT DIS  
 SECT/NASHVILLE//TN/37212  
 Journal: INFECTION AND IMMUNITY, 1996, V64, N11 (NOV), P4501-4507  
 ISSN: 0019-9567  
 Language: ENGLISH Document Type: ARTICLE  
 Abstract: Helicobacter pylori strains possessing cagA are associated with peptic ulceration . To understand the regulation of expression of cagA, picB, associated with interleukin-8 induction, and ureA, encoding

the small urease subunit, we created gene fusions of *cagA*, *ureA*, and *picB* of strain 3401, using a promoterless reporter (*xylE*). Expression of *XylE* after growth in broth culture revealed that basal levels of expression of *cagA* and *ureA* in *H. pylori* were substantially greater than for *picB*. For *cagA* expression in stationary-phase cells, brief exposure to acid pH caused a significant increase in *xylE* expression compared with neutral pH. In contrast, expression of *xylE* in *ureA* or *picB* decreased after parallel exposure to acid pH (pH 7 > 6 > 5 > 4), regardless of the growth phase. Expression of the CagA protein varied with growth phase and pH exposure in parallel with the observed transcriptional variation. The concentration of CagA in a cell membrane-enriched fraction after growth at pH 6 was significantly higher than after growth at pH 5 or 7. We conclude that the promoterless reporter *xylE* is useful for studying the regulation of gene expression in *H. pylori* and that regulation of CagA production occurs mainly at the transcriptional level.

6/AB/33 (Item 7 from file: 34)  
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci  
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05220676 Genuine Article#: VH958 Number of References: 68  
Title: SOLITARY VIEWS OF THE STOMACH (Abstract Available)  
Author(s): BLUM AL  
Corporate Source: HOP CANTONAL UNIV GENEVA, DEPT MED INTERNE, DIV  
GASTROENTEROL/CH-1011 LAUSANNE//SWITZERLAND/  
Journal: DIGESTION, 1996, V57, N5 (SEP), P287-298  
ISSN: 0012-2823  
Language: ENGLISH Document Type: ARTICLE  
Abstract: Technology has propelled gastric physiology and pathophysiology since 1825, the year when the French Academy of Science tried to attribute a prize to the best paper on digestive physiology. I have analyzed the contributions of Ismar Boas, as well as my personal experience in studying gastric mucosal permeability, gastric secretion, a vaccine directed against *Helicobacter pylori* and the metabolism of this pathogen. In addition, I have examined the interplay between sociopolitical events and research activities, the role of suppressed minorities in research, the fallacies of falsification strategies, the dependence of valid results from unorthodox experimental approaches and creative elements. Some of the older gastric researchers expressed solitary views - an attitude which may have helped them to make novel and valid observations.

6/AB/34 (Item 8 from file: 34)  
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

04508786 Genuine Article#: TH574 Number of References: 27  
Title: *HELICOBACTER-PYLORI* VACCINE - STATUS AND IMPLICATIONS FOR  
DRUG-THERAPY OF ULCER DISEASE (Abstract Available)  
Author(s): CHEN MH  
Corporate Source: SUN YAT SEN UNIV MED SCI, ZHONGSHAN RD 2/CANTON//PEOPLES R  
CHINA/  
Journal: CLINICAL IMMUNOTHERAPEUTICS, 1995, V4, N6 (DEC), P420-424  
ISSN: 1172-7039  
Language: ENGLISH Document Type: ARTICLE  
Abstract: *Helicobacter pylori* is now accepted as the aetiological agent in peptic ulcer disease and has been characterised as a grade 1 carcinogen. The development of an effective vaccine is therefore

desirable, although effective therapies for the eradication of the organism are available. The first step towards the development of an anti- *H. pylori* vaccine was initiated by the demonstration that a sonicate of *H. felis* can protect mice against infection with *H. felis*. Urease has been identified in the mouse model as a protective antigen, Ether virulence factors, such as vacuolate cytotoxin and a heat shock protein of *H. pylori*, have been investigated as candidate vaccine components by the development of a new *H. pylori* mouse model. Vaccine adjuvants, delivery systems and therapeutic vaccination are likely to be the areas of major progress in the future.

6/AB/35 (Item 9 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv..

04333162 Genuine Article#: RW006 Number of References: 37  
Title: CONTRIBUTION OF UREASE TO ACID TOLERANCE IN YERSINIA-ENTEROCOLITICA  
(Abstract Available)

Author(s): DEKONINGWARD TF; ROBINSBROWNE RM

Corporate Source: ROYAL CHILDRENS HOSP, DEPT MICROBIOL & INFECT  
DIS, FLEMINGTON RD/PARKVILLE/VIC 3052/AUSTRALIA/; ROYAL CHILDRENS  
HOSP, DEPT MICROBIOL & INFECT DIS/PARKVILLE/VIC 3052/AUSTRALIA/; UNIV  
MELBOURNE, DEPT MICROBIOL/PARKVILLE/VIC 3052/AUSTRALIA/

Journal: INFECTION AND IMMUNITY, 1995, V63, N10 (OCT), P3790-3795

ISSN: 0019-9567

Language: ENGLISH Document Type: ARTICLE

Abstract: The stomach serves as a barrier to enteric infection because of the antibacterial effect of the hydrochloric acid in gastric juice. In this study, we tested the ability of the enteric pathogen *Yersinia enterocolitica* to tolerate a pH range of 2.0 to 6.0 and found that under the conditions of a normal human fasting stomach (pH < 3 and a gastric emptying time of 2 h), *Y. enterocolitica* is highly acid resistant, showing approximately 85% survival. The resistance of *Y. enterocolitica* to acid in vitro depended on the bacterial growth phase and the concentration of urea in the medium, being maximal during stationary phase in the presence of at least 0.3 mM urea. Urease -negative mutants of *Y. enterocolitica* were constructed by disrupting the urease gene complex of a virulent strain of serogroup O9. Compared with the wild type, these mutants showed an approximately 1,000-fold decrease in the ability to tolerate acid in vitro (<0.08% survival) and a 10-fold reduction in viability after passage through the stomachs of mice. Complementation of the disrupted urease genes in trans restored the ability of urease -negative mutants to tolerate low pH in vitro and gastric acidity to approximately wild-type levels. These findings indicate that urease is responsible for acid resistance in *Y. enterocolitica* and suggest that urease contributes to the virulence of *Y. enterocolitica* by enhancing the likelihood of bacterial survival during passage through the stomach.

6/AB/36 (Item 10 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

03439567 Genuine Article#: PD890 Number of References: 52  
Title: HELICOBACTER-PYLORI AND MOLECULAR-BIOLOGY - VIRULENCE FACTORS,  
DIAGNOSIS, AND VACCINE DEVELOPMENT (Abstract Available)

Author(s): SUERBAUM S

Corporate Source: RUHR UNIV BOCHUM, INST MED MIKROBIOL & IMMUNOL/D-44780

BOCHUM//GERMANY/

Journal: IMMUNITAT UND INFEKTION, 1994, V22, N4 (AUG), P137-141

ISSN: 0340-1162

Language: GERMAN Document Type: REVIEW

Abstract: The discovery of H.pylori as the etiologic agent of chronic antral type B gastritis and the finding that H.pylori is involved in the pathogenesis of gastroduodenal ulcer disease and gastric carcinoma have triggered intensive research about this organism. After overcoming considerable initial difficulties, researchers succeeded in adapting the instruments of molecular biology to the study of this highly fastidious organism. This has led to a rapid increase of knowledge concerning the basis of H.pylori virulence (as well as that of the related animal pathogens H.mustelae and H.felis) and to the development of molecular methods for the purposes of diagnosis and epidemiological research. The latest application of molecular biology in this area is the use of recombinant proteins for the development of an H.pylori vaccine. This review gives an overview of this rapidly developing field.

6/AB/37 (Item 11 from file: 34)

DIALOG(R) File 34:SciSearch(R) Cited Ref Sci

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02804182 Genuine Article#: ME638 Number of References: 0  
(NO REFS KEYED)

Title: DEVELOPMENT OF A VACCINE AGAINST HELICOBACTER-PYLORI - A SHORT  
OVERVIEW (Abstract Available)

Author(s): RAPPUOLI R; BUGNOLI M; GHIARA P; COVACCI A; OLIVIERI R; XIANG ZY  
; TELFORD JL

Corporate Source: IMMUNOBIOLOG RES INST SIENA, VIA FIORENTINA 1/I-53100  
SIENA//ITALY/

Journal: EUROPEAN JOURNAL OF GASTROENTEROLOGY & HEPATOLOGY, 1993, V5, S2 (OCT), PS76-S78

ISSN: 0954-691X

Language: ENGLISH Document Type: ARTICLE

Abstract: Aim: Growing evidence that gastric and duodenal disease is caused by Helicobacter pylori infection suggests that this disease may be prevented by vaccination. We therefore assessed the possibilities for development of a vaccine.

Method: Survey of published studies.

Present state of development: Development of a vaccine requires identification of the factors responsible for bacterial virulence and disease induction and large-scale production and testing of potential vaccines in animal models. So far several factors involved in bacterial adhesion, colonization and virulence have been identified. Among these, the most promising candidates for vaccine development are the adhesins, the vacuolating cytotoxin and urease. Urease-based vaccines have shown some promising results in protecting mice against H. felis infection.

Proposals: The unique features of H. pylori infection and disease formation in man suggest that vaccines should be tested in models more relevant to humans, and that the vacuolating cytotoxin and the cytotoxin-associated gene A (cagA) should be seriously considered as vaccine candidates. This hypothesis is supported by the recent observation that only the subset of strains that produce the vacuolating cytotoxin and cagA are associated with disease.

6/AB/38 (Item 12 from file: 34)  
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
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00858085 Genuine Article#: FB988 Number of References: 51  
 Title: SHUTTLE CLONING AND NUCLEOTIDE-SEQUENCES OF *HELICOBACTER-PYLORI*  
 GENES RESPONSIBLE FOR UREASE ACTIVITY (Abstract Available)  
 Author(s): LABIGNE A; CUSSAC V; COURCOUX P  
 Corporate Source: INST PASTEUR, INSERM, UNITE ENTEROBACTERIES, U199/F-75724  
 PARIS 15//FRANCE/  
 Journal: JOURNAL OF BACTERIOLOGY, 1991, V173, N6, P1920-1931  
 Language: ENGLISH Document Type: ARTICLE  
 Abstract: Production of a potent urease has been described as a trait common to all *Helicobacter pylori* so far isolated from humans with gastritis as well as peptic ulceration. The detection of urease activity from genes cloned from *H. pylori* was made possible by use of a shuttle cosmid vector, allowing replication and movement of cloned DNA sequences in either *Escherichia coli* or *Campylobacter jejuni*. With this approach, we cloned a 44-kb portion of *H. pylori* chromosomal DNA which did not lead to urease activity when introduced into *E. coli* but permitted, although temporarily, biosynthesis of the urease when transferred by conjugation to *C. jejuni*. The recombinant cosmid (pILL585) expressing the urease phenotype was mapped and used to subclone an 8.1-kb fragment (pILL590) able to confer the same property to *C. jejuni* recipient strains. By a series of deletions and subclonings, the urease genes were localized to a 4.2-kb region of DNA and were sequenced by the dideoxy method. Four open reading frames were found, encoding polypeptides with predicted molecular weights of 26,500 (ureA), 61,600 (ureB), 49,200 (ureC), and 15,000 (ureD). The predicted UreA and UreB polypeptides correspond to the two structural subunits of the urease enzyme; they exhibit a high degree of homology with the three structural subunits of *Proteus mirabilis* (56% exact matches) as well as with the unique structural subunit of jack bean urease (55.5% exact matches). Although the UreD-predicted polypeptide has domains relevant to transmembrane proteins, no precise role could be attributed to this polypeptide or to the UreC polypeptide, which both mapped to a DNA sequence shown to be required to confer urease activity to a *C. jejuni* recipient strain.

6/AB/39 (Item 1 from file: 71)  
 DIALOG(R)File 71:ELSEVIER BIOBASE  
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01396664 2000072798  
 Pilot study of phoP/phoQ-deleted *Salmonella enterica* serovar typhimurium expressing *Helicobacter prior*i urease in adult volunteers  
 Angelakopoulos H.; Hohmann E.L.  
 ADDRESS: E.L. Hohmann, Infectious Diseases Division, Gray/Jackson 504,  
 Department of Medicine, Boston, MA 02114, United States  
 EMAIL: ehohmann@partners.org  
 Journal: Infection and Immunity, 68/4 (2135-2141), 2000, United States  
 CODEN: INFIB  
 ISSN: 0019-9567  
 DOCUMENT TYPE: Article  
 LANGUAGES: English SUMMARY LANGUAGES: English  
 NO. OF REFERENCES: 30

Attenuated *Salmonella enterica* serovar Typhi has been studied as an oral vaccine vector. Despite success with attenuated *S. enterica* serovar Typhimurium vectors in animals, early clinical trials of *S. enterica*

serovar Typhi expressing heterologous antigens have shown that few subjects have detectable immune responses to vectored antigens. A previous clinical study of phoP/phoQ-deleted *S. enterica* serovar Typhi expressing *Helicobacter pylori* urease from a multicopy plasmid showed that none of eight subjects had detectable immune responses to the vectored antigen. In an attempt to further define the variables important for engendering immune responses to vectored antigens in humans, six volunteers were inoculated with  $5 \times 10^7$  to  $8 \times 10^7$  CFU of phoP/phoQ-deleted *S. enterica* serovar Typhimurium expressing the same antigen. Two of the six volunteers had fever; none had diarrhea, bacteremia, or other serious side effects. The volunteers were more durably colonized than in previous studies of phoP/phoQ-deleted *S. enterica* serovar Typhi. Five of the six volunteers seroconverted to *S. enterica* serovar Typhimurium antigens and had strong evidence of anti-Salmonella mucosal immune responses by enzyme-linked immunospot studies. Three of six (three of five who seroconverted to Salmonella) had immune responses in the most sensitive assay of urease-specific immunoglobulin production by blood mononuclear cells in vitro. One of these had a fourfold or greater increase in end-point immunoglobulin titer in serum versus urease. Attenuated *S. enterica* serovar Typhimurium appears to be more effective than *S. enterica* serovar Typhi for engendering immune responses to urease. Data suggest that this may be related to a greater stability of antigen-expressing plasmid in *S. enterica* serovar Typhimurium and/or prolonged intestinal colonization. Specific factors unique to nontyphoidal salmonellae may also be important for stimulation of the gastrointestinal immune system.

6/AB/40 (Item 2 from file: 71)  
DIALOG(R) File 71:ELSEVIER BIOBASE  
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00439042 96132926  
Immunogenicity and safety of recombinant *Helicobacter pylori* urease in a nonhuman primate  
Stadtlander C.T.K.-H.; Gangemi J.D.; Khanolkar S.S.; Kitsos C.M.; Farris H.E. Jr.; Fulton L.K.; Hill J.E.; Huntington F.K.; Lee C.K.; Monath T.P.  
ADDRESS: Dr. C.T.K.-H. Stadtlander, Greenville Hospital System, Clemson Unive. Biomed. Cooperative, Box 34 19 12, Clemson, SC 29634-1912, United States  
Journal: Digestive Diseases and Sciences, 41/9 (1853-1862), 1996, United States  
PUBLICATION DATE: 19960000  
CODEN: DDSCD  
ISSN: 0163-2116  
DOCUMENT TYPE: Article  
LANGUAGES: English SUMMARY LANGUAGES: English

Groups of squirrel monkeys (*Saimiri* spp.), predetermined to be free of *Helicobacter* infections in the gastric mucosa, were immunized orally with 0.5-4.5 mg of *Helicobacter pylori* recombinant urease (rUrease) and 25-500 mug of *Escherichia coli* heat-labile enterotoxin (LT) adjuvant. Oral immunization with rUrease resulted in a markedly elevated serum immunoglobulin G (IgG) antibody response with peak levels at 45 days after immunization. No significant gastric inflammation or cytotoxicity was evident in rUrease immunized monkeys as determined by light and electron microscopy. Twenty-five micrograms of LT was a sufficient and safe adjuvant dosage, whereas higher dosages resulted in diarrhea and lethargy. Animals developed a serum IgG antibody response to LT that did not impede the production of anti-rUrease antibody levels. The results of this investigation indicate that rUrease is immunogenic in a nonhuman primate.



6/AB/41 (Item 1 from file: 73)  
 DIALOG(R)File 73:EMBASE  
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10583238 EMBASE No: 2000048045  
 Accuracy of sup 1sup 3C-urea breath test in clinical use for diagnosis of  
 Helicobacter pylori infection  
 Riepl R.L.; Folwaczny C.; Otto B.; Klauser A.; Blendinger C.; Wiebecke B.  
 ; Konig A.; Lehnert P.; Heldwein W.  
 Dr. R.L. Riepl, Medizinische Klinik, Klinikum Innenstadt, Ludwig  
 Maximilians-Univ. Munchen, Ziemssenstrasse 1, D-80336 Munchen Germany  
 Zeitschrift fur Gastroenterologie ( Z. GASTROENTEROL. ) (Germany) 2000,  
 38/1 (13-19)  
 CODEN: ZGASA ISSN: 0044-2771  
 DOCUMENT TYPE: Journal; Article  
 LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH; GERMAN  
 NUMBER OF REFERENCES: 37

The sup 1sup 3-urea breath test (UBT) is a noninvasive test for diagnosis of Helicobacter pylori infection of gastric mucosa. The aim of this prospective study was to assess the accuracy of a simple UBT in clinical routine use. Methods: The study population comprised of 100 patients (49 f, 51 m) requiring diagnostic upper GI endoscopy. One biopsy specimen was taken from the gastric antrum, body and fundus, respectively, for standard histological examination and one additional specimen from each location was transformed into transport medium for cultivation of H. pylori. After vaccination of the culture plates the biopsies were tested for urease activity (UAT). After recovery from endoscopy the patients had to pass an one liter endexpiratory breath sample before and 15 min after drinking 200 ml orange juice, pH 3.6. containing 75 mg of sup 1sup 3C-urea. sup 1sup 3C0inf 2 was measured in the breath samples using isotope-selective nondispersive infrared spectrometry. Results: Defining gold standard groups with all biopsy tests (from antrum and corpus) positive or negative the sup 1sup 3C0inf 2 delta over baseline (DOB) cut-off level of UBT was set at 6.5% in order to best discriminate positive from negative patients (ROC analysis). UBT was positive in 37% of all subjects. Taken UAT and histological examination together (positive when both tests were positive) UBT displayed a sensitivity of 92%, a specificity of 94%, a positive predictive value of 89%, and a negative predictive value of 94%. When including the results of culture sensitivity and negative predictive value reached almost 100%. The mean of the sup 1sup 3C0inf 2-DOB values from H. pylori-positive duodenal or gastric ulcer patients did not differ from controls (H. pylori-positive patients without lesions). The sup 1sup 3C0inf 2-DOB values of the ulcer group were correlated significantly with the active inflammatory component of gastritis in antrum, corpus, and fundus. Conclusion: UBT with this setup detects H. pylori infection in clinical routine use with high accuracy. The increase of exhaled sup 1sup 3C0inf 2 does not predict ulcer disease but reflects the degree of active inflammation of gastric mucosa.

6/AB/42 (Item 2 from file: 73)  
 DIALOG(R)File 73:EMBASE  
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06577958 EMBASE No: 1996242531  
 Prospects for improved therapy for Helicobacter pylori infection  
 Hua-Xiang Xia H.; Talley N.J.  
 Clinical Sciences Building, Department of Medicine, Nepean Hospital, PO  
 Box 63, Penrith, NSW 2751 Australia

Expert Opinion on Investigational Drugs ( EXPERT OPIN. INVEST. DRUGS ) ( United Kingdom) 1996, 5/8 (959-976)  
CODEN: EOIDE ISSN: 1354-3784  
DOCUMENT TYPE: Journal; Review  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Cure of *Helicobacter pylori* infection has been recommended for patients with peptic ulcer disease. However, an optimal treatment regimen has not been defined. Dual therapy regimens with omeprazole and amoxycillin or clarithromycin usually achieve eradication rates of 70-80%, while a combination of ranitidine bismuth citrate and clarithromycin produces eradication rates of over 80%. Triple therapy with a bismuth salt plus metronidazole and tetracycline or amoxycillin (the standard bismuth-based triple therapy), or a proton pump inhibitor (PPI-based therapy) plus two antimicrobial agents (metronidazole, amoxicillin or clarithromycin) is effective in eradicating *H. pylori*, with eradication rates of over 90% for metronidazole-sensitive strains. Drug resistance and compliance influence the clinical efficacy. Addition of a PPI to bismuth-based triple therapy (quadruple therapy) may overcome drug resistance, reduce side-effects, and shorten the treatment duration, but compliance may be reduced. Therefore, the search for a simple and effective therapy continues. Novel approaches include alternative types of drug administration (topical or parenteral), substitution with more powerful analogues or novel agents such as enzyme-inhibitors, Chinese herbs, honey, lactic acid and unsaturated fatty acids. Recently, vaccines against *H. pylori* infection have been developed and tested in animal models. The studies have demonstrated that oral immunisation with *H. pylori* whole cell sonicates or recombinant urease of the organism not only prevents the infection but can also eradicate it. Thus, therapeutic vaccines, which we believe are achievable, may finally eliminate *H. pylori* from the human stomach, and therefore cure most peptic ulcer disease.

6/AB/43 (Item 3 from file: 73)  
DIALOG(R)File 73:EMBASE  
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06133473 EMBASE No: 1995165582

Adjuvant therapy for *Helicobacter pylori* eradication: Role of lansoprazole shown in vitro

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Laboratoire de Bacteriologie, Hopital Pellegrin, Universite Bordeaux II, Place Amelie Raba Leon, 33076 Bordeaux Cedex France

Journal of Clinical Gastroenterology ( J. CLIN. GASTROENTEROL. ) (United States) 1995, 20/SUPPL. 1 (S24-S27)

CODEN: JCGAD ISSN: 0192-0790

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The recognition of *Helicobacter pylori* (*H. Pylori*) as a major cause of gastroduodenal diseases has led to the use of antibiotics to treat these diseases. However, antibiotics used alone are not very effective, and adjuvant therapy is required. The most potent adjuvant therapy consists of increasing the stomach pH with proton pump inhibitors (PPIs). In addition to this action on stomach pH, PPIs, and especially lansoprazole, have been found to have antimicrobial activity against *H. pylori*. At high concentrations, they are even bactericidal. Furthermore, they can inhibit *H. pylori* urease activity. These properties, as well as their antisecretory activity, provide the grounds for their use in eradication of *H. pylori*.

6/AB/44 (Item 4 from file: 73)  
 DIALOG(R)File 73:EMBASE  
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06005668 EMBASE No: 1995034320  
 An update on Helicobacter pylori  
 Wadstrom T.  
 Department of Medical Microbiology, Lund University, Solvegatan 23,S-223  
 62 Lund Sweden  
 Current Opinion in Gastroenterology ( CURR. OPIN. GASTROENTEROL. ) ( United Kingdom) 1995, 11/1 (69-75)  
 CODEN: COGAE ISSN: 0267-1379  
 DOCUMENT TYPE: Journal; Review  
 LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Because of the limitations of animal models and the question of relevance of various in vitro observations, much controversy remains about the pathogenic mechanisms by which Helicobacter pylori can induce disease. Like those of other bacterial pathogens, the putative virulence factors of H. pylori can be divided into three groups: colonization factors, disease-inducing factors, and factors promoting persistence. Colonization factors allow the pathogen to become established in the host and include motility, urease production, and adhesion mechanisms. Disease-inducing factors consist of cytotoxins and urease, disruption of the gastric mucosal barrier, induction of inflammatory mediators, production of changed gastric physiology and possibly strain specific ulcerogenic properties. Finally, the importance of H. pylori infection may be due to its capacity for long-term persistence. An H. pylori infection can be considered a slow adaptive process. The mechanisms by which this pathogen survives and interacts with the host immune system may provide a model for other persistent mucosal pathogens. Eradication of H. pylori is now accepted therapy for peptic ulcer and may lead to elimination of a major risk factor for gastric malignancies.

6/AB/45 (Item 1 from file: 76)  
 DIALOG(R)File 76:Life Sciences Collection  
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01887667 3693842  
 The new path to preventing ulcers  
 Tompkins, L.S.; Falkow, S.  
 SCIENCE (WASH.) vol. 267, no. 5204, pp. 1621-1622 (1995)  
 ISSN: 0036-8075  
 DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH  
 SUBFILE: Microbiology Abstracts B: Bacteriology; Medical and Pharmaceutical Biotechnology Abstracts

The close relation between Helicobacter infection, ulcers, and now stomach cancers has been ratified by a select panel of the National Institutes of Health. Helicobacter pylori is now on the list of microbial agents that are classified as carcinogens because of its close association with two types of gastric cancers. Infection of the stomach with H. pylori can occur as early as infancy. The research group reporting the new mouse model previously treated mice acutely with H. pylori to examine the role of VacA- and CagA-associated factors in the pathogenesis of the disease. Mice orally immunized with Helicobacter antigens, including VacA and urease, were protected from subsequent challenge with viable type I H. pylori strains. These results suggest not only that vaccination might indeed prevent Helicobacter infection, but also that it provides a

relatively cheap and simple model to identify other factors, including the CagA-associated gene products, that may be useful as vaccine antigens.

6/AB/46 (Item 1 from file: 144)  
DIALOG(R) File 144:Pascal  
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14955955 PASCAL No.: 01-0108387

Evaluation of factors that can affect protective immune responses following oral immunization of recombinant *Helicobacter pylori* urease apoenzyme

JANG SEONG KIM; JI HOON CHANG; EUN JEONG PARK; SOO IL CHUNG; JUNG SUN YUM  
Mogam Biotechnology Research Institute, 341 Pojung-Ri, Koosung-Myon, Yongin, Kyonggi-Do 449-910, Korea, Republic of  
Journal: Journal of microbiology and biotechnology, 2000, 10 (6) 865-872  
Language: English

*Helicobacter pylori* is the major cause of gastritis, peptic ulcer, and a principal risk factor for gastric cancer. As the first step towards a vaccine against *H. pylori* infection, *H. pylori* urease was expressed and purified as a recombinant apoenzyme (rUrease) in *E. coli*. In order to develop an effective immunization protocol using rUrease, the host immune responses were evaluated after the oral immunization of mice with rUrease preparations plus cholera toxin relative to various conditions, such as the physical nature of the antigen, the frequency of the booster immunization, the dose of the antigen, and the route of administration. The protective efficacy was assessed using a quantitative culture following an *H. pylori* SS1 challenge. It was demonstrated that rUrease, due to its particulate nature, was more superior than the UreB subunit as a vaccine antigen. The oral immunization of rUrease elicited significant systemic and secretory antibody responses, and activated predominantly Th2-type cellular responses. The bacterial colonization was significantly reduced (similar 100-fold) in those mice immunized with three or four weekly oral doses of rUrease plus cholera toxin ( $p < 0.05$ ), when compared to the non-immunized/challenged controls. The protection correlated well with the elicited secretory IgA level against rUrease, and these secretory antibody responses were highly dependent on the frequency of the booster immunization, yet unaffected by the dose of the antigen (25-200  $\mu$ g). These results demonstrate the remarkable potential of rUrease as a vaccine antigen, thereby strengthening the possibility of developing an *H. pylori* vaccine for humans.

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6/AB/47 (Item 2 from file: 144)  
DIALOG(R) File 144:Pascal  
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14653147 PASCAL No.: 00-0325168

Accuracy of SUP 1 SUP 3 C-urea breath test in clinical use for diagnosis of *Helicobacter pylori* infection

RIEPL R L; FOLWACZNY C; OTTO B; KLAUSER A; BLENDINGER C; WIEBECKE B; KOENIG A; LEHNERT P; HELDWEIN W

Medizinische Klinik, Klinikum Innenstadt, Ludwig-Maximilians-Universitaet Muenchen, Muenchen, Germany; Pathologisches Institut, Klinikum Innenstadt, Ludwig-Maximilians-Universitaet Muenchen, Muenchen, Germany; Max-von-Pettenkofer-Institut, Muenchen, Germany

Journal: Zeitschrift fuer Gastroenterologie, 2000, 38 (1) 13-19

Language: English Summary Language: German

The SUP 1 SUP 3 C-urea breath test (UBT) is a noninvasive test for

diagnosis of *Helicobacter pylori* infection of gastric mucosa. The aim of this prospective study was to assess the accuracy of a simple UBT in clinical routine use. Methods: The study population comprised of 100 patients (49 f, 51 m) requiring diagnostic upper GI endoscopy. One biopsy specimen was taken from the gastric antrum, body and fundus, respectively, for standard histological examination and one additional specimen from each location was transformed into transport medium for cultivation of *H. pylori*. After vaccination of the culture plates the biopsies were tested for urease activity (UAT). After recovery from endoscopy the patients had to pass an one liter endexpiratory breath sample before and 15 min after drinking 200 ml orange juice, pH 3.6, containing 75 mg of SUP 1 SUP 3 C-urea. SUP 1 SUP 3 CO SUB 2 was measured in the breath samples using isotope-selective nondispersive infrared spectrometry. Results: Defining gold standard groups with all biopsy tests (from antrum and corpus) positive or negative the SUP 1 SUP 3 CO SUB 2 delta over baseline (DOB) cut-off level of UBT was set at 6.5% in order to best discriminate positive from negative patients (ROC analysis). UBT was positive in 37% of all subjects. Taken UAT and histological examination together (positive when both tests were positive) UBT displayed a sensitivity of 92%, a specificity of 94%, a positive predictive value of 89%, and a negative predictive value of 94%. When including the results of culture sensitivity and negative predictive value reached almost 100%. The mean of the SUP 1 SUP 3 CO SUB 2 -DOB values from *H. pylori*-positive duodenal or gastric ulcer patients did not differ from controls (*H. pylori*-positive patients without lesions). The SUP 1 SUP 3 CO SUB 2 -DOB values of the ulcer group were correlated significantly with the active inflammatory component of gastritis in antrum, corpus, and fundus. Conclusion; UBT with this setup detects *H. pylori* infection in clinical routine use with high accuracy. The increase of exhaled SUP 1 SUP 3 CO SUB 2 does not predict ulcer disease but reflects the degree of active inflammation of gastric mucosa.

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6/AB/48 (Item 3 from file: 144)  
 DIALOG(R) File 144:Pascal  
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13167943 PASCAL No.: 97-0429764

Proprietes fonctionnelles et immunologiques de la chaperonine HspA de *Helicobacter pylori*

(Immunological and functional properties of the chaperonin HspA of *helicobacter pylori*)

KANSAU SILVA Imad Nasib; LABIGNE A, dir

Universite de Paris 07, Paris, Francee

Univ.: Universite de Paris 07. Paris. FRA Degree: Th. doct.

1996-07; 1996 256 p.

Language: French Summary Language: French; English

*Helicobacter pylori* est une bacterie responsable de gastrites chroniques qui peuvent evoluer vers la maladie ulcereuse, l'atrophie gastrique et les carcinomes gastriques. L'objectif de ce travail a ete de caracteriser la chaperonine HspA (homologue a GroES) de *H. pylori* sur le plan genetique, moleculaire et immunologique. La caracterisation de l'operon codant pour HspA et HspB (homologue a GroEL) a revele une organisation similaire a celle des operons groESL d'autres bacteries. HspA s'est averee unique du fait de la presence, dans sa partie C-terminale, d'une sequence riche en residus histidine. La construction de proteines recombinantes contenant differents fragments de HspA fusionnees a la proteine MBP et l'etude de leur affinite pour divers cations divalents ont permis de demontrer que HspA presente une plus forte affinite pour les ions nickel que pour les autres cations; la fixation du nickel a lieu sur la

partie C-terminale de HspA. La co-expression du gene hspA et des genes ureasiques de *H. pylori* chez *Escherichia coli* a confirme le role de HspA dans l'activation de l' urease . Par ailleurs, il a ete montre que HspA est immunogene et que la reponse serique des patients infectes est dirigee principalement contre sa partie N-terminale. Neanmoins, seule une partie des patients infectes produit des anticorps anti-HspA. L'analyse de la sequence en acides amines de la proteine codee par des isolats cliniques a revele l'existence de deux variants antigeniques. Cependant, aucune correlation n'a pu etre observee entre la presence de chacun de ces variants et la production d'anticorps. Enfin, dans un modele murin, HspA augmente les proprietes protectrices de la fraction UreB de la preparation vaccinale . L'ensemble des donnees acquises a permis d'esquisser un premier modele fonctionnel du role de HspA vis-a-vis de l' urease . Les donnees immunologiques presentees ouvrent des perspectives pour la recherche des moyens de protection contre l'infection a *H. pylori*

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6/AB/49 (Item 4 from file: 144)  
DIALOG(R)File 144:Pascal  
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12619005 PASCAL No.: 96-0308028  
Therapeutic immunization against *Helicobacter mustelae* in naturally infected ferrets  
CUENCA R; BLANCHARD T G; CZNN S J; NEDRUD J G; MONATH T P; LEE C K;  
REDLINE R W  
Department of Pediatrics, Case Western Reserve University, Cleveland,  
Ohio, United States  
Journal: *Gastroenterology* : (New York, NY. 1943), 1996, 110 (6)  
1770-1775

Language: English  
Background & Aims : *Helicobacter* infection of the gastric antrum is responsible for a number of gastric disorders. Antibiotic therapy is lengthy and is not always effective. It has been shown previously that oral immunization against *Helicobacter felis* in mice can prevent colonization after challenge. The aim of this study was to investigate the efficacy of therapeutic immunization in eradicating an established *Helicobacter* infection and in reducing gastritis . Methods : Domestic ferrets, confirmed to be infected with *Helicobacter mustelae* by gastric endoscopy, were orally immunized with varying doses of purified *Helicobacter pylori* urease in combination with the mucosal adjuvant cholera toxin. Ferrets were assessed 1 week and 6 weeks after treatment for infection and pathology. Results : Therapeutic immunization eradicated *Helicobacter* colonization in 30% of all immunized ferrets, although there was no difference in efficacy between the varying doses of antigen tested. The difference was statistically significant when compared with animals administered cholera toxin alone or buffer ( $P = 0.04$ ). The intensity of inflammation was also significantly reduced in immunized animals ( $P = 0.0003$ ). Conclusions : Oral immunization with purified *H. pylori* urease and cholera toxin can eradicate *H. mustelae* in a natural host pathogen model. Oral immunization of chronically infected animals markedly reduced gastric inflammation.

6/AB/50 (Item 5 from file: 144)  
DIALOG(R)File 144:Pascal  
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12313354 PASCAL No.: 95-0550809

Vaccine strategies for prevention fo helicobacter pylori infection  
SELLMAN S; BLANCHARD T G; NEDRUD J G; CZINN S J  
AXON Anthony T R, ed; BLASER M J, ed; KIMURA Ken, ed; MEGRAUD Francis, ed  
; SHIMOYAMA Takashi, ed; SIPPONEN P, ed; WYLE F A, ed  
Case western reserve univ., dep. pediatrics, Cleveland OH 44106, USA  
General infirmary, cent. digestive diseases, Leeds, United Kingdom;  
Groupe hosp. Pellegrin, lab. bacteriologie enfants, 33076 Bordeaux, France  
International symposium on Helicobacter pylori and its diseases, 7 (   
Tokyo JPN) 1994-04-18  
Journal: European journal of gastroenterology & hepatology, 1995, 7 (   
SUP1) S1-S6

Language: English

Objectives: To examine the level and duration of the humoral immune response to Helicobacter felis following oral immunization or infection. Design and methods: Germ-free mice were orally immunized with sonicated H . felis plus cholera toxin five times over 6 weeks. One week after immunization was completed, immunized and control non-immunized mice received an oral challenge of live H . felis organisms. The animals were killed at 3-week intervals and serum, gastric washings, intestinal washings and gastric biopsies were obtained. H . felis infection was confirmed by a positive urease test or culture of the gastric biopsy. Serum gastric and intestinal antibody titers were determined by enzyme-linked immunosorbent assay. Conclusion: Infection and immunization against H . felis produces a specific humoral response. The humoral response in infection alone is significantly smaller than that of immunized animals until 6 weeks after infection. The humoral response following oral immunization persists for at least 18 weeks without further stimulation. The presence of an H . felis-specific antibody immune response before infection may be needed to protect animals from acute Helicobacter infection.

6/AB/51 (Item 6 from file: 144)  
DIALOG(R)File 144:Pascal  
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11491518 PASCAL No.: 94-0329560  
Lack of protection against gastric helicobacter infection following immunisation with jack bean urease : the rejection of a novel hypothesis  
MINHU CHEN; LEE A; HAZELL S L; PINJIN HU; YIYANG LI  
Univ. New South Wales, school microbiology immunology, Kensington N.S.W.  
2033, Australia  
Journal: FEMS microbiology letters, 1994, 116 (3) 245-250  
Language: English

6/AB/52 (Item 1 from file: 351)  
DIALOG(R)File 351:Derwent WPI  
(c) 2002 Thomson Derwent. All rts. reserv.

013515584  
WPI Acc No: 2000-687530/200067  
XRAM Acc No: C00-209315  
Product comprising a synergistic combination of HpaA and HOP38 polypeptides, or fusion polypeptides, useful for treating or reducing the risk of Helicobacter pylori infection  
Patent Assignee: ASTRAZENECA AB (ASTR )  
Inventor: PAPPO J  
Number of Countries: 092 Number of Patents: 002  
Patent Family:  
Patent No Kind Date Applicat No Kind Date Week

WO 200066624 A1 20001109 WO 2000SE808 A 20000428 200067 B  
 AU 200047894 A 20001117 AU 200047894 A 20000428 200111

Priority Applications (No Type Date): SE 991548 A 19990429

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 200066624 A1 E 65 C07K-014/205

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY CA CH  
 CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE  
 KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU  
 SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR  
 IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 200047894 A C07K-014/205 Based on patent WO 200066624

Abstract (Basic): WO 200066624 A1

Abstract (Basic):

NOVELTY - A pharmaceutical product comprising polypeptides for simultaneous or sequential administration to a mammal for preventing or treating *Helicobacter pylori* infection, is new.

DETAILED DESCRIPTION - A pharmaceutical product comprising polypeptides for simultaneous or sequential administration to a mammal for preventing or treating *Helicobacter pylori* infection, is new, where:

(a) the first polypeptide comprises a sequence identical or similar to, residues 21-270 of a 270 amino acid sequence, residues 24-273 of either of two 273 amino acid sequences, or residues 1-250 of a 277 amino acid sequence, all fully defined in the specification; and

(b) the second polypeptide comprises a sequence identical or similar to, residues 28-260 of a 260 amino acid sequence, residues 28-260 of either of two 260 amino acid sequences, residues 1-233 of a 268 amino acid sequence, or residues 53-97 of a 97 amino acid sequence, all fully defined in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) a fusion polypeptide for use in preventing or treating *Helicobacter pylori* infection, comprising the two amino acid sequences of the novelty;

(2) a vaccine comprising the fusion polypeptide of (1) and a mucosal adjuvant and/or delivery system.

(3) a nucleic acid encoding the fusion polypeptide of (1), and comprising:

(a) a first nucleotide sequence identical or similar to, residues 61-777 of an 813 nucleotide sequence, residues 70-786 of either of two 822 nucleotide sequences, and nucleotides 82-798 of an 831 nucleotide sequence, all fully defined in the specification; and

(b) a second nucleotide sequence identical or similar to residues 873-1572 of a 1670 nucleotide sequence, residues 873-1572 of a 1670 nucleotide sequence; residues 82-783 of a 783 nucleotide sequence, residues 106-804 of an 804 nucleotide sequence, and residues 157-294 of a 294 nucleotide sequence.

ACTIVITY - Antibacterial.

Groups of mice were immunized intranasally with (A) purified recombinant HpaA (182 micro-g), (B) purified recombinant HOP38 (182 micro-g), (C) both HpaA and HOP38 (91 micro-g of each), (D) *Helicobacter pylori* whole cell lysate (100 micro-g), or (E) buffer. Immunizations were performed in the presence of CT adjuvant (10 micro-g). For HpaA, a polypeptide comprising residues 20-260 of a 260 amino acid sequence, fully defined in the specification, but with threonine at position 223 instead of alanine, was used. For HOP38, a polypeptide comprising residues 24-262 of a 273 amino acid sequence, fully defined in the specification, was used. Treatment of pre-existing



H . pylori infection was assessed by quantitative urease 2 weeks after experimental challenge with 10 to the power 6 colony forming units of H . pylori SSI by gavage. Mice were immunized at weekly intervals for 4 weeks. Half the total volume of the formulation was administered into each nostril. Two weeks after the last immunization, mice were sacrificed and stomach tissue harvested for quantitative urease assay. Results for the extent of H . pylori infection (by urease assay) were, for (A) 2.91E+04 +/-19624; (B) 3.87E+04 +/-35590; (C) 6.43E+03 +/-5495; (D) 3.40+03 +/-1838; and (E) 7.87E+04 +/-60473.

MECHANISM OF ACTION - Synergist; vaccine.

USE - For preventing or treating Helicobacter pylori infection.  
pp; 65 DwgNo 0/0

6/AB/53 (Item 2 from file: 351)  
DIALOG(R)File 351:Derwent WPI  
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012999349

WPI Acc No: 2000-171201/200015

XRAM Acc No: C00-053281

Use of Lactobacillus-derived urease , as a vaccine for preventing or treating Helicobacter infection and conditions including gastric ulcer , gastritis and gastric cancer caused by the infection

Patent Assignee: CHEIL JEDANG CORP (CHEI-N)

Inventor: PARK J B

Number of Countries: 081 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200003730	A1	20000127	WO 98KR216	A	19980716	200015 B
AU 9884643	A	20000207	AU 9884643	A	19980716	200029
			WO 98KR216	A	19980716	

Priority Applications (No Type Date): WO 98KR216 A 19980716

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 200003730 A1 E 38 A61K-039/07

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU  
CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS  
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
TT UA UG US UZ VN YU ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR  
IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9884643 A A61K-039/07 Based on patent WO 200003730

Abstract (Basic): WO 200003730 A1

Abstract (Basic):

NOVELTY - A vaccine for generating protective immunity against Helicobacter (Hb) infection in a mammalian host comprises a polyaminoacid preparation including epitopes exhibited by a Lactobacillus (Lb)-derived urease in combination with a carrier or diluent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine for inducing a passively protective potency against Hb infection in mammals comprising Lb-derived urease-specific IgA antibody to the passive protective potency with a carrier, the antibody being produced from a mammalian host immunized with the urease which is able to produce a protective immune response against Hb infection;

(2) a process for assaying protective response in a mammal infected with Hb organism comprising determining the presence of antibody

reactive with epitopes exhibited by (Lb)-derived urease endogenous to the Hb organism within a sample collected from a gastric biopsy of the mammal.

ACTIVITY - Antibacterial; Antiulcer; Antiinflammatory; Cytostatic.

MECHANISM OF ACTION - Vaccine . Lactobacillus fermentum (LF) ATCC 11739 was cultured and urease fractions were isolated. Mice were orally immunized with 30micro-g of purified LF urease coupled to 1mg of hydroxyapatite plus 10micro-g of cholera toxin adjuvant at day 0, 7, 14, and 21. At day 28, 30 and 32, mice were challenged with 108 H . felis (HF). For comparison purpose, similar SPF BALB/c mice were orally immunized with whole LF lysate (sonicate) and 10micro-g of cholera toxin at day 0, 7, 14 and 21. To evaluate the protection against HF colonization, gastric biopsies from each animal were screened for the presence of HF by assessing urease activity by the CLO test. The results showed that the oral immunization of mice with LF urease affords a statistically significant protection, compared to the immunization of mice with LF sonicate or cholera toxin. 7 of 10 mice immunized with LF sonicate and the 10 mice immunized with cholera toxin were infected with HF, only 4 of 10 mice immunized with LF urease were infected with HF. 30% of the mice immunized with LF sonicate and challenged with HF were protected and all of the mice immunized with cholera toxin and challenged with HF were not protected, 60% of the mice immunized with LF urease were protected from HF challenge.

USE - The vaccines are used for the prevention and treatment of Hb infection in mammals. They can be used for treating or preventing gastric ulcer, gastric ulcer, gastritis, gastric cancer, and other conditions which arise as a result of the presence of H. pylori and/or H. heilmanii.

pp; 38 DwgNo 0/2

6/AB/54 (Item 3 from file: 351)  
DIALOG(R)File 351:Derwent WPI  
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011008950

WPI Acc No: 1996-505900/199650

Related WPI Acc No: 1995-006797; 1995-200383

XRAM Acc No: C96-158680

New immunogenic compsn. contg. UreB and HspA antigens of Helicobacter -  
for treatment and prevention of esp. H pylori infection, also new  
antibodies specific for these antigens.

Patent Assignee: INST NAT SANTE & RECH MEDICALE (INRM ); INST PASTEUR  
(INSP )

Inventor: FERRERO R L; LABIGNE A; SUERBAUM S; THIBERGE J

Number of Countries: 070 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9634624	A1	19961107	WO 96EP1834	A	19960502	199650 B
AU 9656934	A	19961121	AU 9656934	A	19960502	199711

Priority Applications (No Type Date): US 95447177 A 19950519; US 95432697 A 19950519

Patent Details:

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AU 9656934 A A61K-039/106 Based on patent WO 9634624

Abstract (Basic): WO 9634624 A

A compsn. (A) comprises a mixture of Helicobacter antigens consisting essentially of UreB and HspA of H. pylori, or peptides with at least 75, pref. 80-90% similarity with them, or their fragments able to elicit antibodies recognised by H. pylori or a cellular response against H. pylori infection. Also new are antibodies (Ab), poly- or mono-clonal, directed against (A).

USE - (A) is useful as a vaccine to protect humans or other animals (esp. cats and dogs) against Helicobacter infection or as therapeutic agents to treat such infections. Partic. they are used to provoke a mucosal response, esp. practically the same response as provided by a total cell extract of the pathogen. Ab can also be used to prevent or treat infections, partic. by H. pylori or H. felis.

ADVANTAGE - (A) is the first recombinant subunit vaccine to induce an immunoprotective response against gastric Helicobacter infection. HspA acts as a chaperonin that increases urease activity and it also enhances protection.

Dwg.0/20

6/AB/55 (Item 1 from file: 357)  
DIALOG(R)File 357:Derwent Biotech Res.  
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0256119 DBA Accession No.: 2000-10609 PATENT  
Method for producing anti-pylorospirbacillus immune eggs - by injecting pyloric helicobacterium urease gene into fowl for vaccine production

AUTHOR: Chen H

CORPORATE SOURCE: People's Republic of China.

PATENT ASSIGNEE: Chinese-Acad.Sci. 2000

PATENT NUMBER: CN 1245011 PATENT DATE: 20000223 WPI ACCESSION NO.:

2000-388171 (2034)

PRIORITY APPLIC. NO.: CN 98117332 APPLIC. DATE: 19980817

NATIONAL APPLIC. NO.: CN 98117332 APPLIC. DATE: 19980817

LANGUAGE: CN

ABSTRACT: A method for producing anti-pyloric helicobacterium immune eggs of fowls, which can be used to cure active gastritis and peptic gastric ulcer as it can suppress the activity and reproduction of pyloric helicobacterium urease (EC-3.5.1.5) is new and involves separating and purifying the expressed product containing pyloric helicobacterium urease gene UreA or UreB in colibacillus to obtain alpha-subunit and beta-subunit of pyloric helicobacterium urease, respectively diluting with buffering liquid of potassium phosphate, adding isovolume F's complete assistant, ultrasonic stirring and injecting it into musculi thoraci of laying fowls. The fowls will lay out said anti-pyloric helicobacterium immuno eggs, whose yolk can be eaten for an immune purpose.

6/AB/56 (Item 2 from file: 357)  
DIALOG(R)File 357:Derwent Biotech Res.  
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0250890 DBA Accession No.: 2000-05380 PATENT  
Use of Lactobacillus-derived urease, as a vaccine for preventing or treating Helicobacter infection and conditions including gastric ulcer, gastritis and gastric cancer caused by the infection - Lactobacillus fermentum culture for urease production and enzyme or enzyme plus cholera toxin fusion protein application in vaccine

AUTHOR: Park J B  
 CORPORATE SOURCE: Seoul, Korea.  
 PATENT ASSIGNEE: Cheil-Jedang 2000  
 PATENT NUMBER: WO 200003730 PATENT DATE: 20000127 WPI ACCESSION NO.:  
 2000-171201 (2015)  
 PRIORITY APPLIC. NO.: WO 98KR00216 APPLIC. DATE: 19980716  
 NATIONAL APPLIC. NO.: WO 98KR216 APPLIC. DATE: 19980716  
 LANGUAGE: English

ABSTRACT: A vaccine for generating protective immunity against Helicobacter infection in a mammalian host comprises a polyamino acid preparation including epitopes exhibited by a Lactobacillus-derived urease (EC-3.5.1.5) in combination with a diluent or adjuvant. Also claimed are: a vaccine for inducing passive protection against Helicobacter infection in mammal comprising Lactobacillus-derived urease -specific IgA antibody (or anti-idiotypic antibody) to the passive protective potency with the adjuvant, the antibody being produced from a mammal host immunized with the urease which is able to produce a protective immune response against Helicobacter infection; and a method for assaying protective response in a mammal infected with Helicobacter sp. involving determining the presence of antibody reactive with epitopes exhibited by Lactobacillus-derived urease endogenous to the Helicobacter organism within a sample collected from a gastric biopsy of the mammal. Lactobacillus fermentum ATCC 11739 or Lactobacillus reuteri can be cultured for urease production and the enzyme may be used alone or as a fusion protein with e.g. cholera toxin in vaccine production. (38pp)

6/AB/57 (Item 3 from file: 357)  
 DIALOG(R)File 357:Derwent Biotech Res.  
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0205065 DBA Accession No.: 97-00186 PATENT  
 Vaccine for inducing mucosal response to Helicobacter containing multimeric urease - Helicobacter pylori recombinant urease production by plasmid pORV214 expression in Escherichia coli, for application as a recombinant vaccine

AUTHOR: Lee C K; Monath T P; Ackerman S K; Thomas Jr W D; Soman G;  
 Kleanthous H; Weltzin R A; Pappo J; Ermak T; Guirakhoo F; Bhagat H;  
 Sussman I

CORPORATE SOURCE: Cambridge, MA, USA.  
 PATENT ASSIGNEE: Oravax 1996  
 PATENT NUMBER: WO 9633732 PATENT DATE: 961031 WPI ACCESSION NO.:  
 96-497373 (9649)

PRIORITY APPLIC. NO.: US 568122 APPLIC. DATE: 951206  
 NATIONAL APPLIC. NO.: WO 96US5800 APPLIC. DATE: 960425  
 LANGUAGE: English

ABSTRACT: A vaccine for inducing a mucosal immune response to Helicobacter comprises, apart from carrier or diluent, multimeric complexes (A) of recombinant, enzymatically inactive Helicobacter urease (EC-3.5.1.5). Also new are a composition for treating gastroduodenal infections containing antigen from the pathogen, and at least one antibiotic, antisecretory, and Bi salt. The vaccines are used to treat or prevent Helicobacter sp., especially Helicobacter pylori infections, and induce a protective, secretory IgA response. A 2.5 kb fragment containing both ureA and ureB gene of H. pylori CPM360 was isolated by the polymerase chain reaction and cloned into plasmid pET24 to form plasmid pORV214. This was used to transform Escherichia coli BL21-DE3. The transformants were cultured, lysed and soluble urease was recovered from the supernatant. Size-exclusion chromatography of the product showed it to exist mainly as the hexamer

(over 70%) and octomer (5-20%). It had no enzymatic activity. (98pp)

6/AB/58 (Item 4 from file: 357)  
 DIALOG(R)File 357:Derwent Biotech Res.  
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0192476 DBA Accession No.: 96-02669 PATENT  
 Vaccine and therapeutic composition containing *Helicobacter pylori* HAP  
 protein - recombinant vaccine production

AUTHOR: Dettmar P W; Smith A W

CORPORATE SOURCE: London, UK.

PATENT ASSIGNEE: Reckitt 1996

PATENT NUMBER: DE 19523554 PATENT DATE: 960104 WPI ACCESSION NO.:  
 96-050293 (9606)

PRIORITY APPLIC. NO.: GB 9413073 APPLIC. DATE: 940629

NATIONAL APPLIC. NO.: DE 4023554 APPLIC. DATE: 950628

LANGUAGE: German

ABSTRACT: A vaccine or therapeutic composition contains *Helicobacter pylori* HAP (hemagglutinin/protease) protein, or a fragment of it. Also disclosed is a 1460 bp DNA sequence and a 256 amino acid protein sequence encoding HAP. HAP, or its fragments, can be a recombinant protein or polypeptide, and preferably fragments contain the zinc-binding region or the protease active site. Compositions may contain 2 or more HAP-related components, optionally also other antigenic compounds from other sources, e.g. from *H. pylori* cytotoxin, heat-shock protein or urease, or cholera toxin subunits. Usual carriers and adjuvants can be included. HAP and its fragments can be made by usual methods of peptide synthesis or by recombinant DNA methods. The compositions are used to treat or prevent infection by *H. pylori* which is implicated in gastric and duodenal ulcers and stomach cancer. (6pp)

6/AB/59 (Item 5 from file: 357)  
 DIALOG(R)File 357:Derwent Biotech Res.  
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0188790 DBA Accession No.: 95-13795 PATENT  
 Composition for treating *Helicobacter* infection - *Helicobacter pylori*  
 recombinant urease monoclonal antibody administered using e.g.  
*Salmonella typhimurium*, *Bacillus* sp., yeast or herpes virus vector, for  
 gastroduodenal disease therapy

AUTHOR: Michetti P; Cortesy-Theulaz I; Blum A; Davin C; Haas R;  
 Kraehen-Buhl J P; Saraga E

PATENT ASSIGNEE: Oravax 1995

PATENT NUMBER: WO 9522987 PATENT DATE: 950831 WPI ACCESSION NO.:  
 95-320292 (9541)

PRIORITY APPLIC. NO.: US 200346 APPLIC. DATE: 940223

NATIONAL APPLIC. NO.: WO 95US2202 APPLIC. DATE: 950223

LANGUAGE: English

ABSTRACT: The following are claimed: (1) the use of a composition, containing *Helicobacter* sp. urease (EC-3.5.1.5) peptide (I), in the production of a medicament for the treatment of a gastroduodenal disease in a mammal; (2) the use of a monoclonal antibody which recognizes *Helicobacter* urease; and (3) compositions containing the ureB subunit of *Helicobacter pylori* urease, a mucosal adjuvant and hydroxyapatite, and containing the ureB subunit in the form of a fusion protein which is genetically linked to the cholera toxin B subunit. Preferably, the composition is contained in a recombinant live vector, or a recombinant carrier system which expresses *Helicobacter* urease

The live vector is selected from *Salmonella typhimurium*, *Salmonella typhi*, *Shigella* sp., *Bacillus* sp., *Lactobacillus* sp., *Mycobacterium bovis* BCG, *Escherichia coli*, *Vibrio cholerae*, *Campylobacter* sp., yeast, herpes virus, adeno virus, polio virus, vaccinia virus and avipox virus. The recombinant carrier system is selected from bluetongue virus-like particles, rota virus-like particles and Ty particles.  
(114pp)

6/AB/60 (Item 6 from file: 357)  
DIALOG(R)File 357:Derwent Biotech Res.  
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0183308 DBA Accession No.: 95-10129

Identification of a novel protective antigen in *Helicobacter felis* - using a monoclonal antibody panel, for potential use in vaccine development  
(conference abstract)

AUTHOR: Blanchard T G; Nedrud J G; Czinn S J

CORPORATE AFFILIATE: Univ.Case-Western-Reserve-Inst.Pathol.

CORPORATE SOURCE: Institute of Pathology, Case Western Reserve University, Cleveland, OH 44106-4943, USA.

JOURNAL: Gut (37, Suppl.1, A31) 1995

ISSN: 0017-5749 CODEN: GUTTAK

CONFERENCE PROCEEDINGS: European *Helicobacter pylori* Study Group, VIIIth International Workshop on Gastro-duodenal Pathology and *Helicobacter pylori*, Edinburgh, Scotland, 7-9 July, 1995.

LANGUAGE: English

ABSTRACT: A panel of 9 *Helicobacter felis*-specific monoclonal antibodies (MAb) was used to identify protective antigens via a passive neutralization experiment which tested for their capacity to protect mice from colonization with the bacterium. Each MAb was incubated with 1 million *H. felis* prior to oral inoculation of mice. One of the MAbs, IgG-50, prevented colonization in 6/7 (86%) inoculated animals as determined by a positive urease (EC-3.5.1.5) reaction by gastric biopsies 1 wk after inoculation. Immunoprecipitation of an *H. felis* protein preparation demonstrated that IgG-50 was specific for a protein of approximately 13 kD. This protein was found to bind nickel using metal chelate chromatography, a characteristic associated with the *H. pylori* heat shock protein-A. However, amino acid analysis of this protein indicated that it was probably distinct from the heat shock protein-A. These data suggest that a low molecular weight protein other than urease may serve as a potential vaccine candidate for *Helicobacter* immunizations. (0 ref)

6/AB/61 (Item 7 from file: 357)  
DIALOG(R)File 357:Derwent Biotech Res.  
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0180821 DBA Accession No.: 95-08841 PATENT

Oral vaccines against *Helicobacter* infections - containing inactivated urease or urease-containing bacterium

AUTHOR: LeVeen H H; Laveen E G; Laveen R F

PATENT ASSIGNEE: LeVeen H H 1995

PATENT NUMBER: EP 654273 PATENT DATE: 950524 WPI ACCESSION NO.: 95-187057 (9525)

PRIORITY APPLIC. NO.: US 185749 APPLIC. DATE: 940124

NATIONAL APPLIC. NO.: EP 94308551 APPLIC. DATE: 941118

LANGUAGE: English

ABSTRACT: Use of a non-enzymatic urease (EC-3.5.1.5) antigen for the production of a medicament for treating and/or preventing infections of

animals and humans caused by *Helicobacter* sp. (especially *Helicobacter pylori*) is claimed. The antigen is preferably an acid urease of bacterial origin (*Lactobacillus fermentum* TK 1214, *Lactobacillus reuteri*, *Lactobacillus ruminis*, *Bacillus* sp. TB-90, *Streptococcus bovis*, *Streptococcus reuteri* or *Streptococcus salivarius*) or plant (jack bean) origin. The antigen has its urease activity inactivated by covalent bonding to increase the mol.wt. and is preferably a glutaraldehyde or formaldehyde inactivated acid urease. Also claimed are: an oral vaccine containing the urease antigen; a composition containing the urease antigen, preferably encapsulated with a peptically resistant material; a vaccine comprising live or killed *L. fermentum* containing the inactive acid urease; use of killed or live bacterium containing the inactivated urease for manufacture of a medicament for oral immunization to urease and inhibition of urea turnover. The antigen can be used in prevention of duodenum ulcers, etc. (12pp)

6/AB/62 (Item 1 from file: 440)  
 DIALOG(R) File 440:Current Contents Search(R)  
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08210076 References: 0

TITLE: Vaccinating against *Helicobacter pylori* infections: Reality and perspectives

AUTHOR(S): Labigne A (REPRINT); Ferrero R; Galmiche JP

CORPORATE SOURCE: INST PASTEUR, INSERM, U389, UNITE PATHOGENIE BACTERIENNE MUQUEUSES, 25 RUE DOCTEUR ROUX/F-75724 PARIS 15//FRANCE/ (REPRINT)

PUBLICATION TYPE: BOOK

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ISBN: 2-7420-0150-6

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The high prevalence of *Helicobacter pylori* infections, the severity of certain associated pathologies (duodenal ulcers, lymphoma, gastric carcinoma) and the predictable gradual emergence of resistance to the antibiotics currently used are factors that have encouraged the development of a vaccine approach to *H. pylori* infections. Studies to date have demonstrated that it is possible to protect animals (mice, ferrets, cats) against *Helicobacter* infection by immunisation via the oral-gastric route using crude extracts of bacterial antigens combined with an adjuvant known to stimulate a mucosal immune response. More recently, better defined *H. pylori* antigens such as the urease subunits, the HspA protein or the VacA cytotoxin, have been identified as possible components of a recombinant subunit vaccine. Progress achieved over the last few years in animal models leads us to expect that a prophylactic and/or therapeutic vaccine will be a reality in the first decade of the 21st century.

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